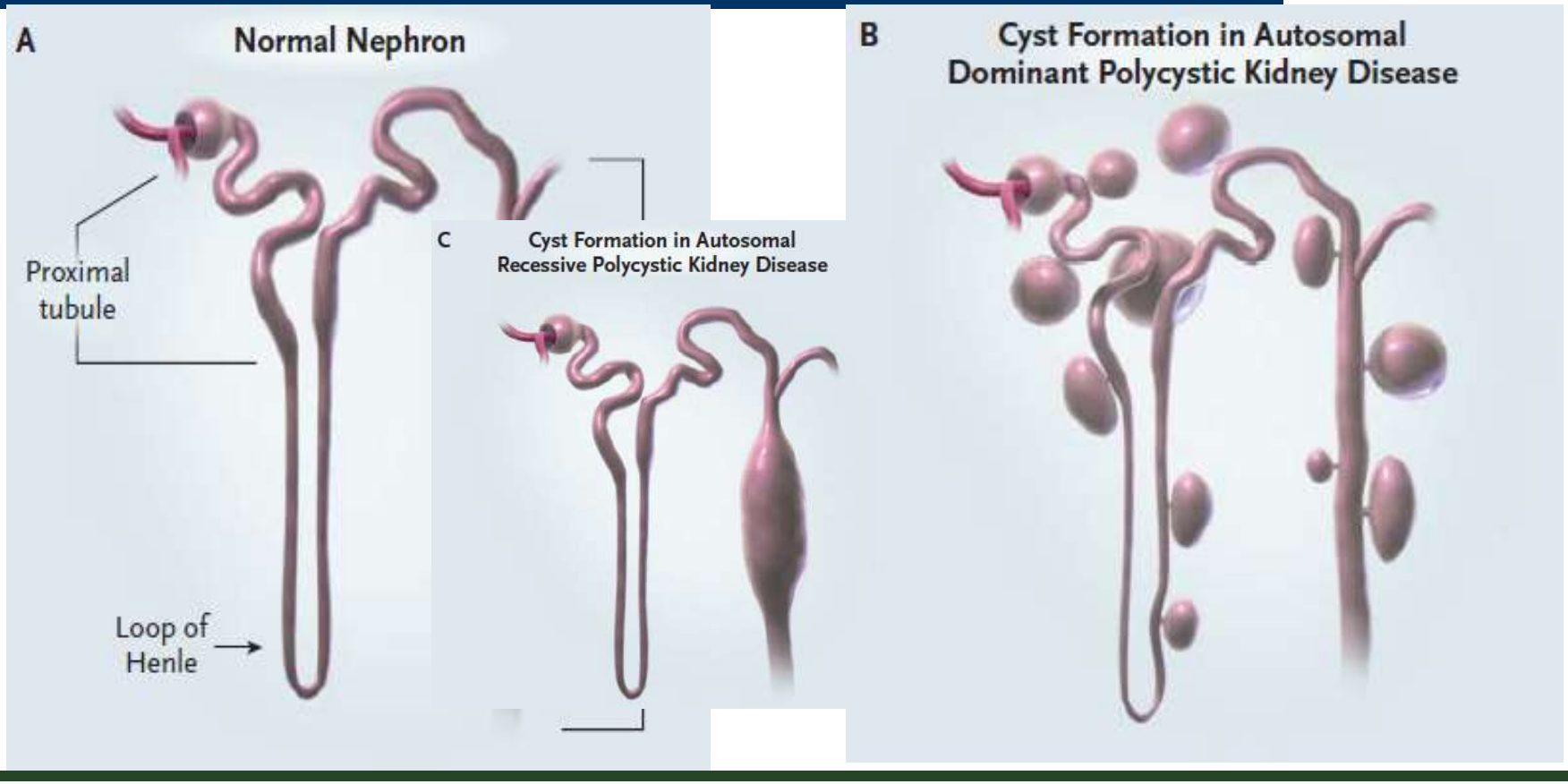
Management of ADPCK:
Where Are We?

Hussein Sheashaa

Professor of Nephrology, Urology and Nephrology Center and Director of Medical E-Learning Unit, Mansoura University

MNDU, Feb 6th, 2015

Introduction



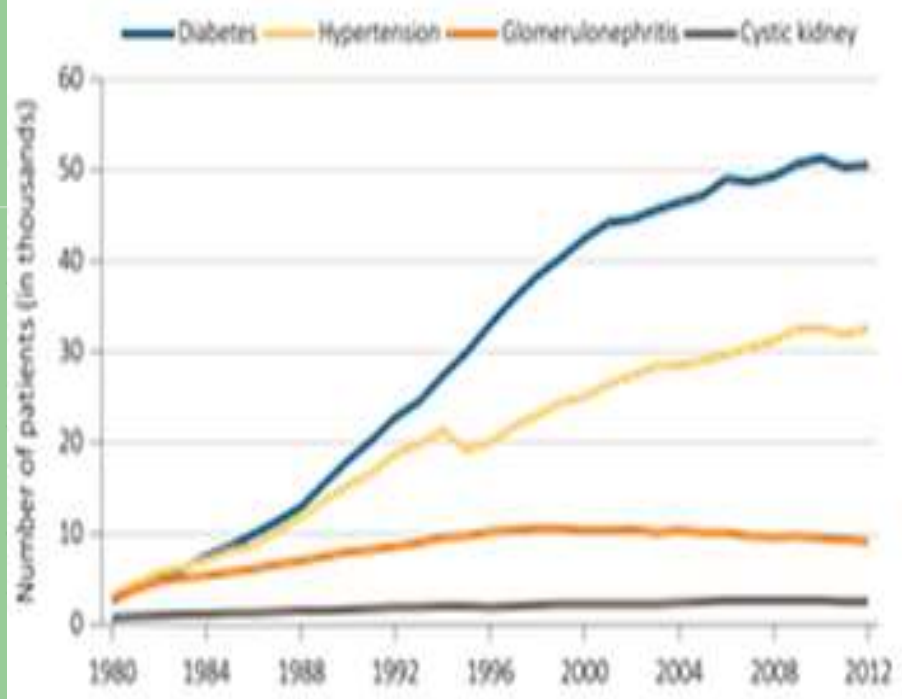
N Engl J Med (2004);350:151-64.

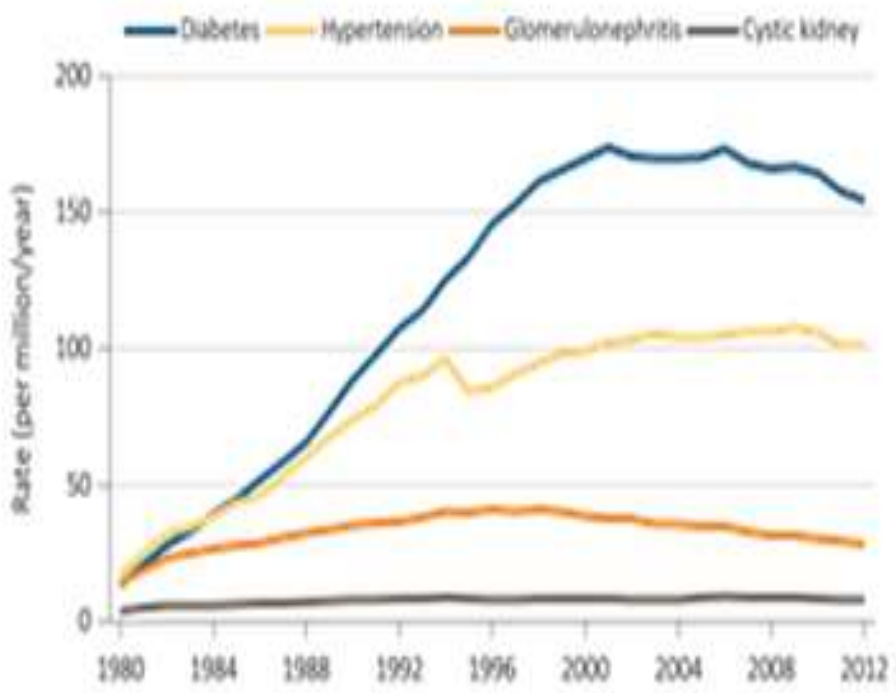
Symptoms

Symptom	Direct	Indirect
Abdominal symptoms	Pain (cyst bleed, infection, stone, other, non-PKD) Chronic vs episodic pain Fullness, early satiety Perception of size, body image Reflux, nausea, vomiting Constipation, bowel symptoms	Inadequate protein-calorie intake
Urinary symptoms	Polyuria Nocturia Dysuria Hematuria	—
Back pain	(Cyst bleed, infection, stone, other, non-PKD) Chronic vs episodic pain	—
Sleep disturbance		Insomnia
Respiratory symptoms	Dyspnea Orthopnea	—
General signs and symptoms	—	Hypertension Headaches Depression Worry

Am J Kidney Dis. (Dec 2013);62(6):1046-1057

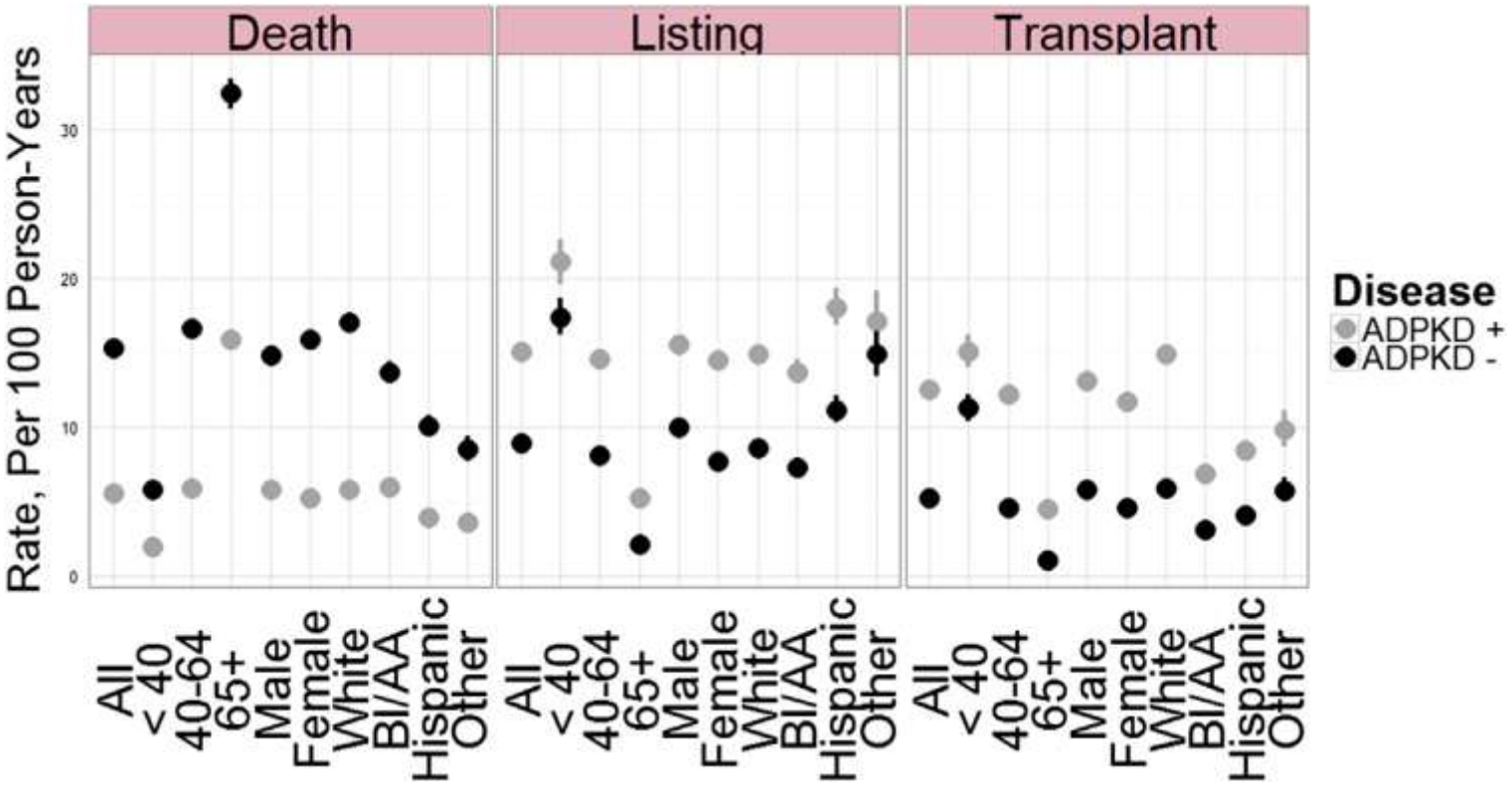
USRDS





USRDS
UNITED STATES RENAL DATA SYSTEM
2014 ANNUAL DATA REPORT

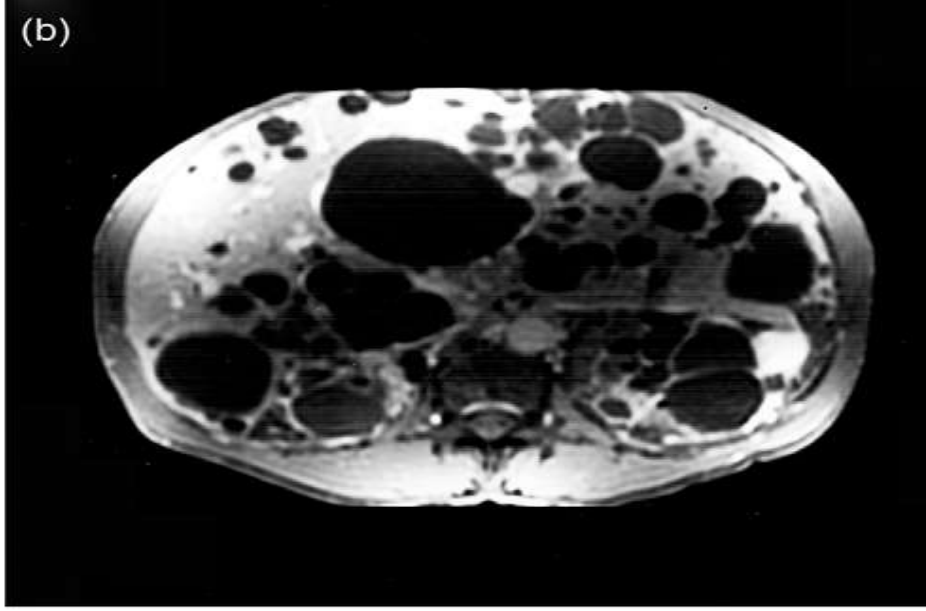
USRDS

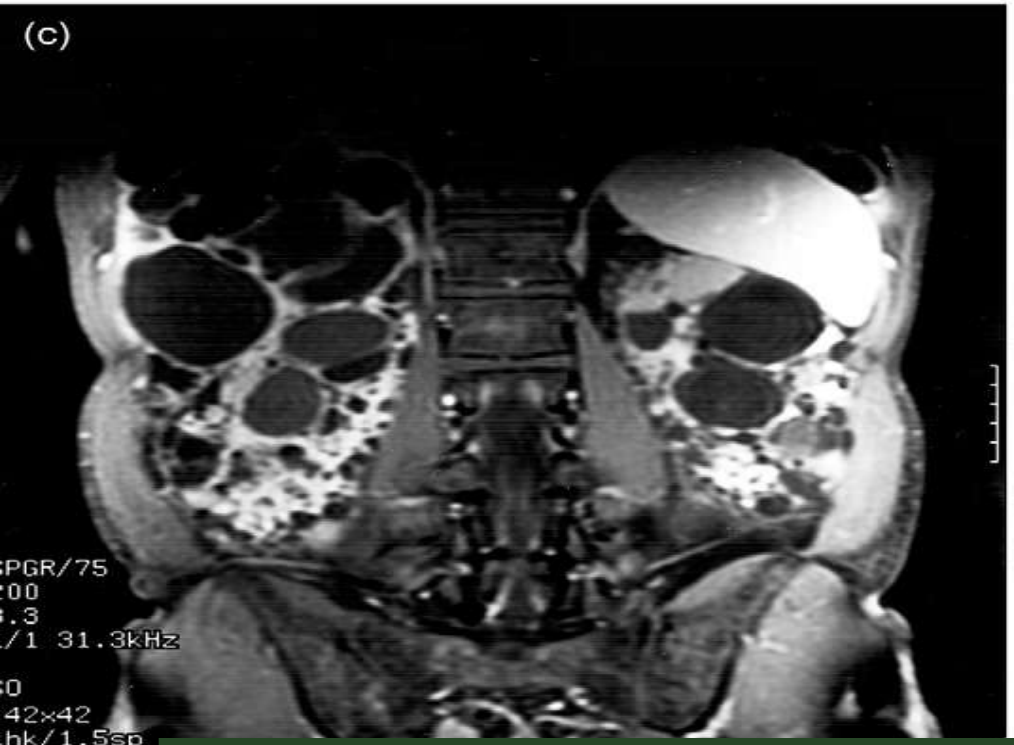


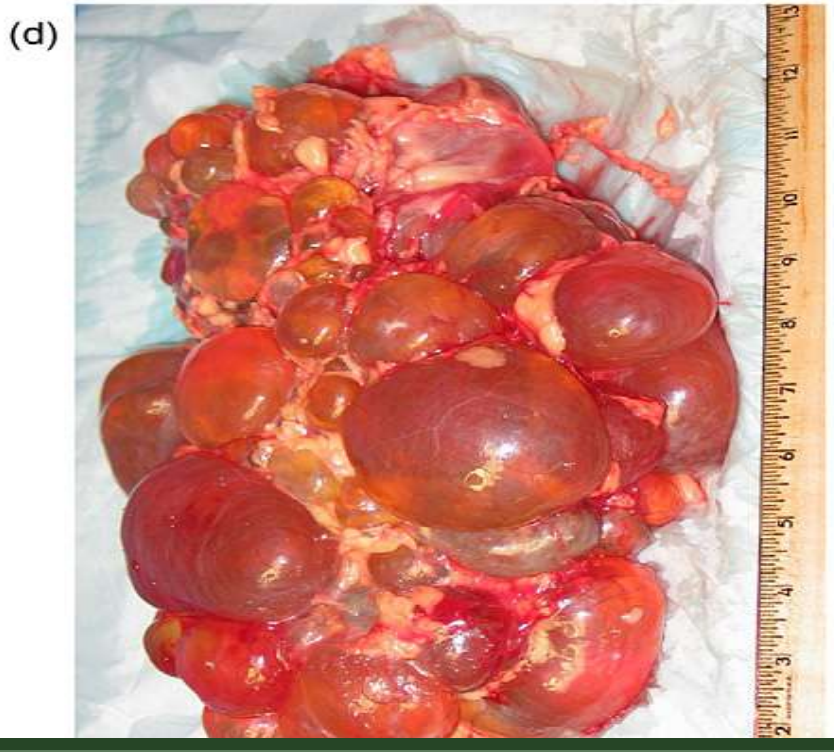
Am J Kidney Dis. 2014;64(4):592-599

US

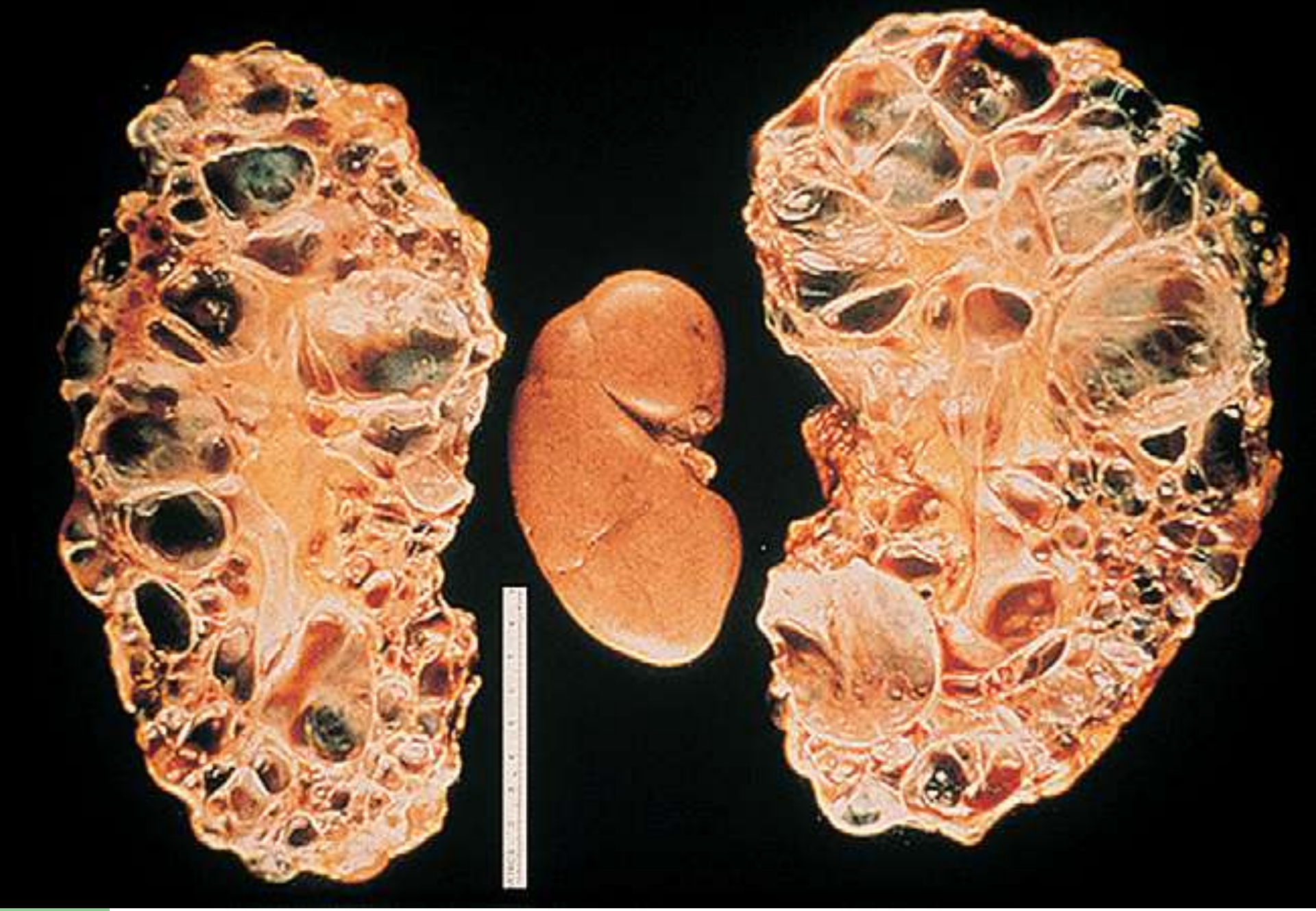
Age (years)	Criteria	PPV	NPV
Original Ravine's PKD1 Diagnostic Criteria			
15-29	≥2 cysts, unilateral or bilateral	99	88
30-39	≥2 cysts in each kidney	100	88
40-59	≥2 cysts in each kidney	100	95
≥60	≥4 cysts in each kidney	100	100
Revised Unified Diagnostic Criteria			
15-29	≥3 cysts, unilateral or bilateral	100	86
30-39	≥3 cysts, unilateral or bilateral	100	86
40-59	≥2 cysts in each kidney	100	95
≥60	≥4 cysts in each kidney	100	100



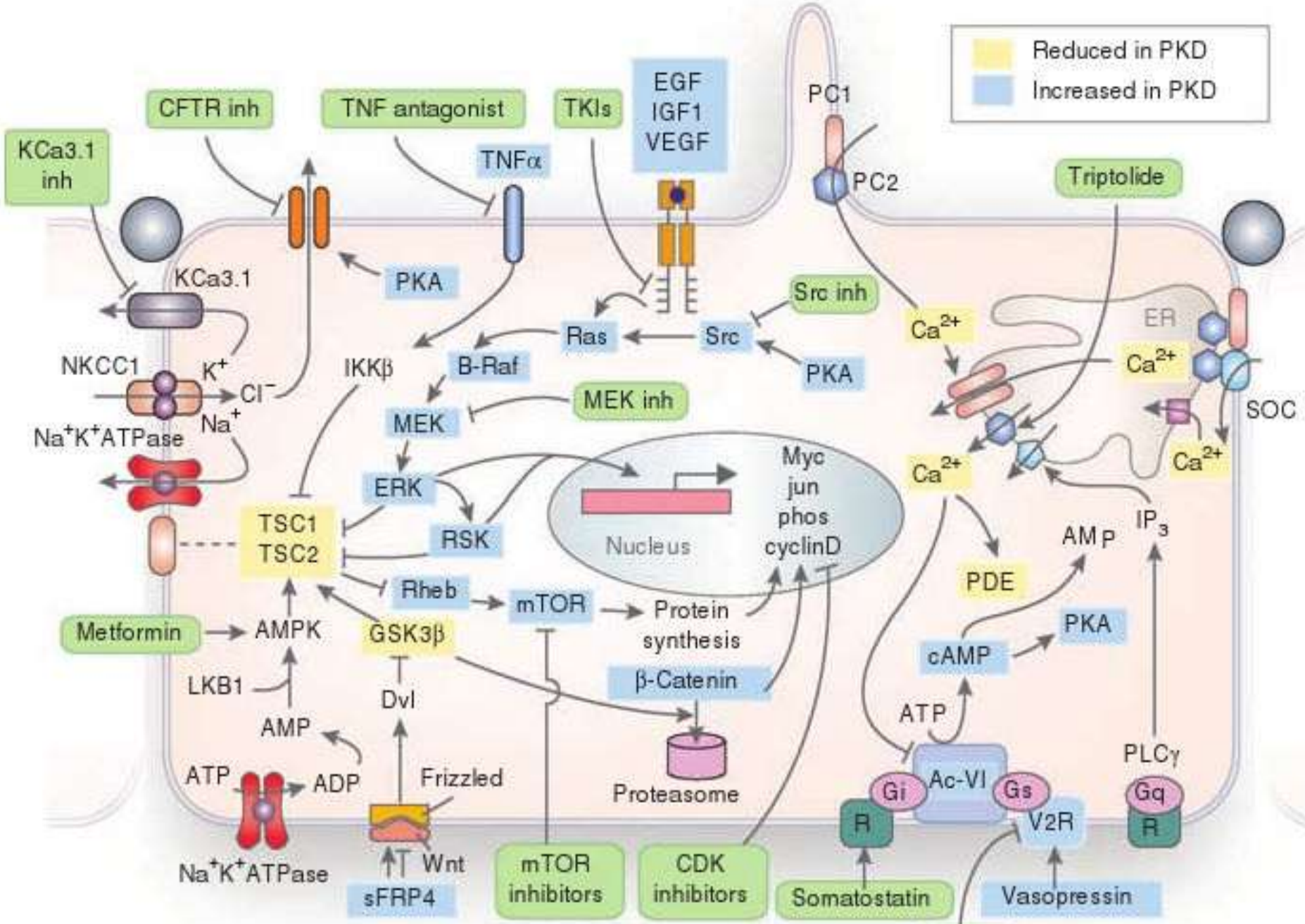




Seldin and Giebisch's The Kidney, Fifth Edition. 2013 Elsevier Inc

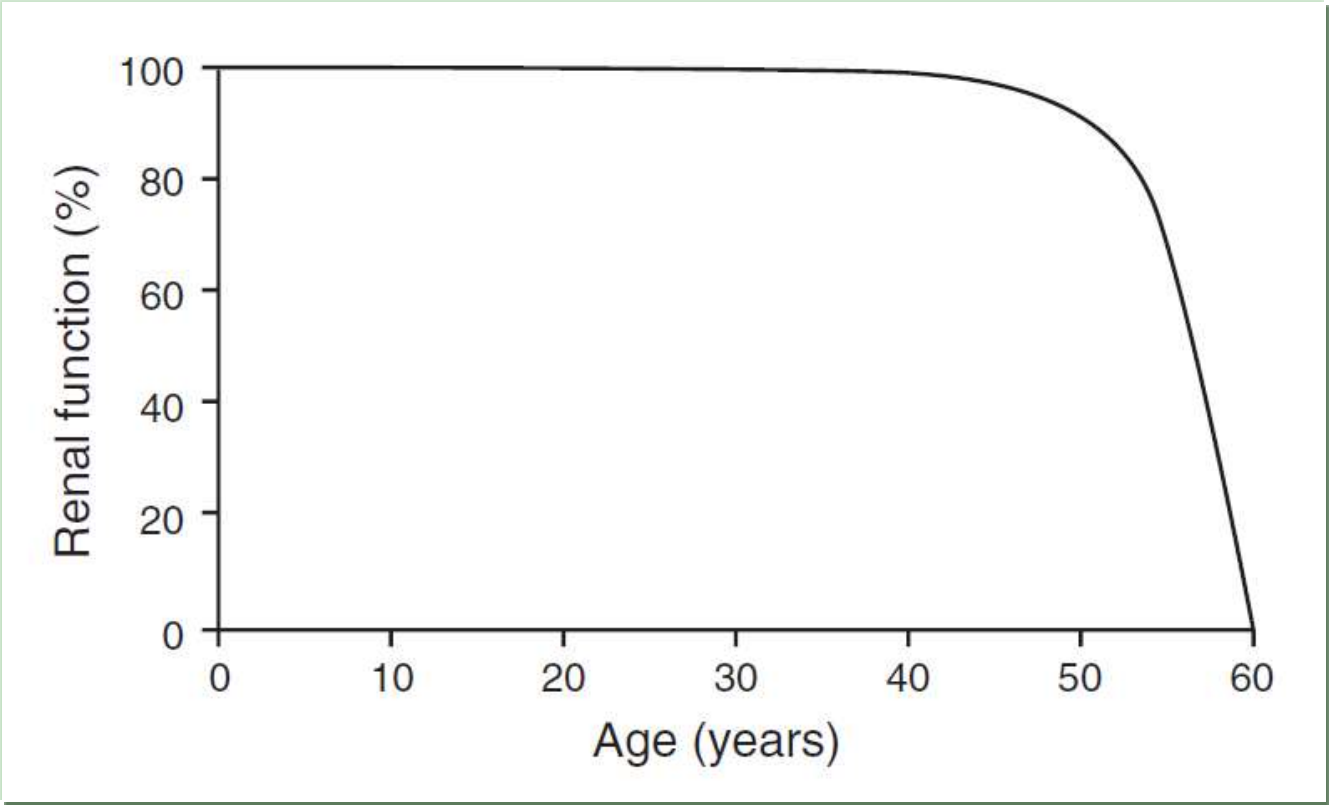


Comprehensive textbook of Nephrology 2010 ed



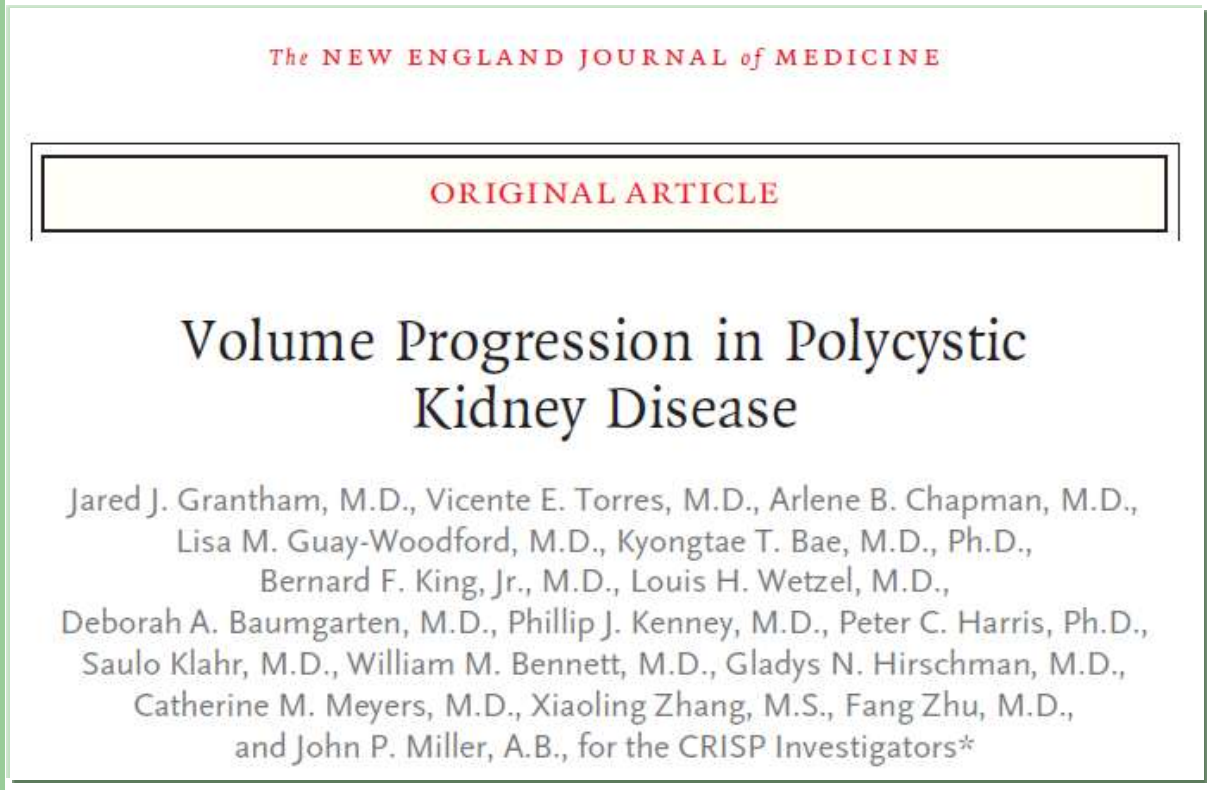
Kidney International (2009), 76:149-168.

Which Outcome to Be Considered?



Clin J Am Soc Nephrol (2008) 3: 1197–1204.

Which Outcome to Be Considered?



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

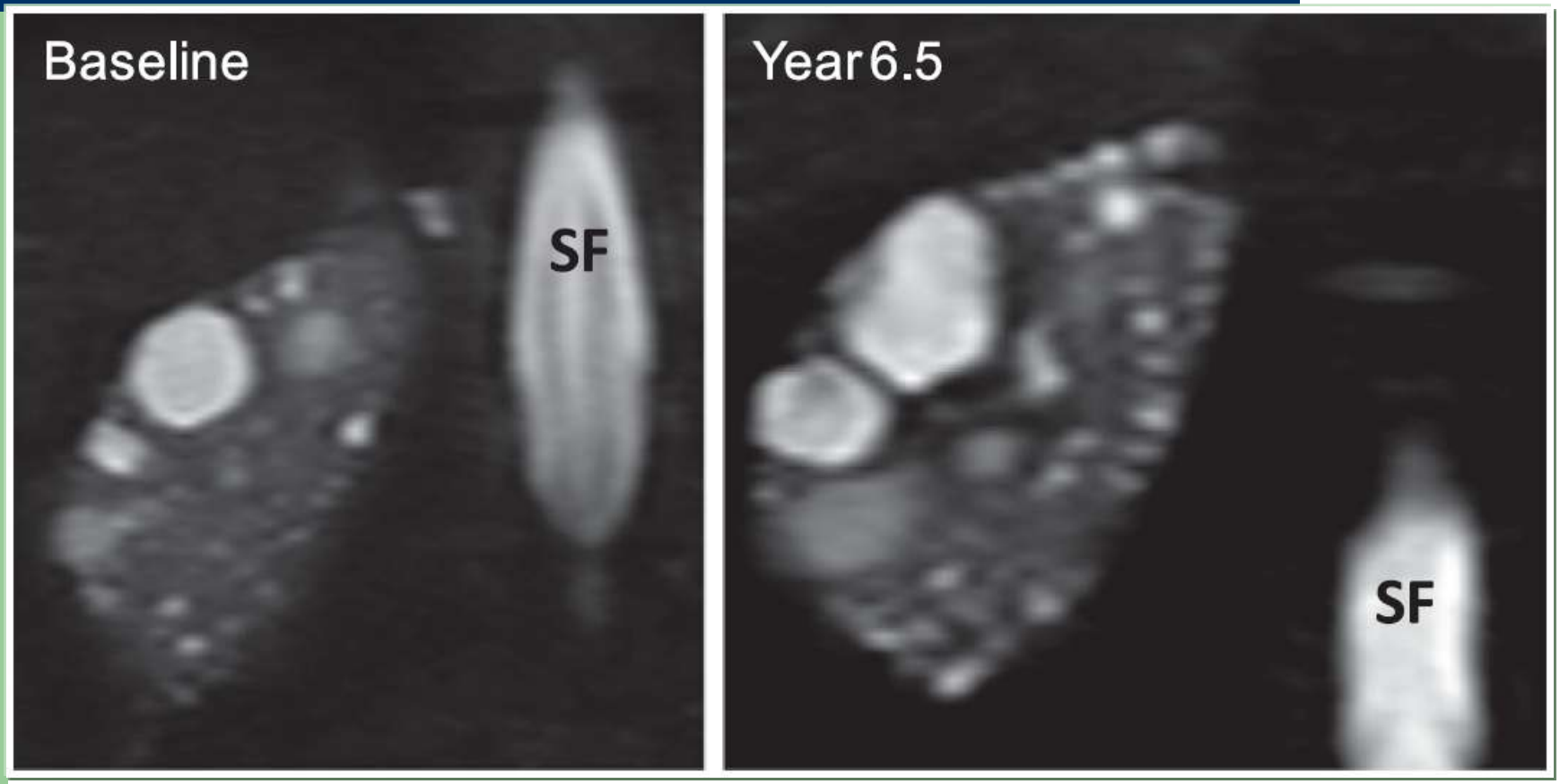
Volume Progression in Polycystic Kidney Disease

Jared J. Grantham, M.D., Vicente E. Torres, M.D., Arlene B. Chapman, M.D., Lisa M. Guay-Woodford, M.D., Kyongtae T. Bae, M.D., Ph.D., Bernard F. King, Jr., M.D., Louis H. Wetzel, M.D., Deborah A. Baumgarten, M.D., Phillip J. Kenney, M.D., Peter C. Harris, Ph.D., Saulo Klahr, M.D., William M. Bennett, M.D., Gladys N. Hirschman, M.D., Catherine M. Meyers, M.D., Xiaoling Zhang, M.S., Fang Zhu, M.D., and John P. Miller, A.B., for the CRISP Investigators*

CRISP

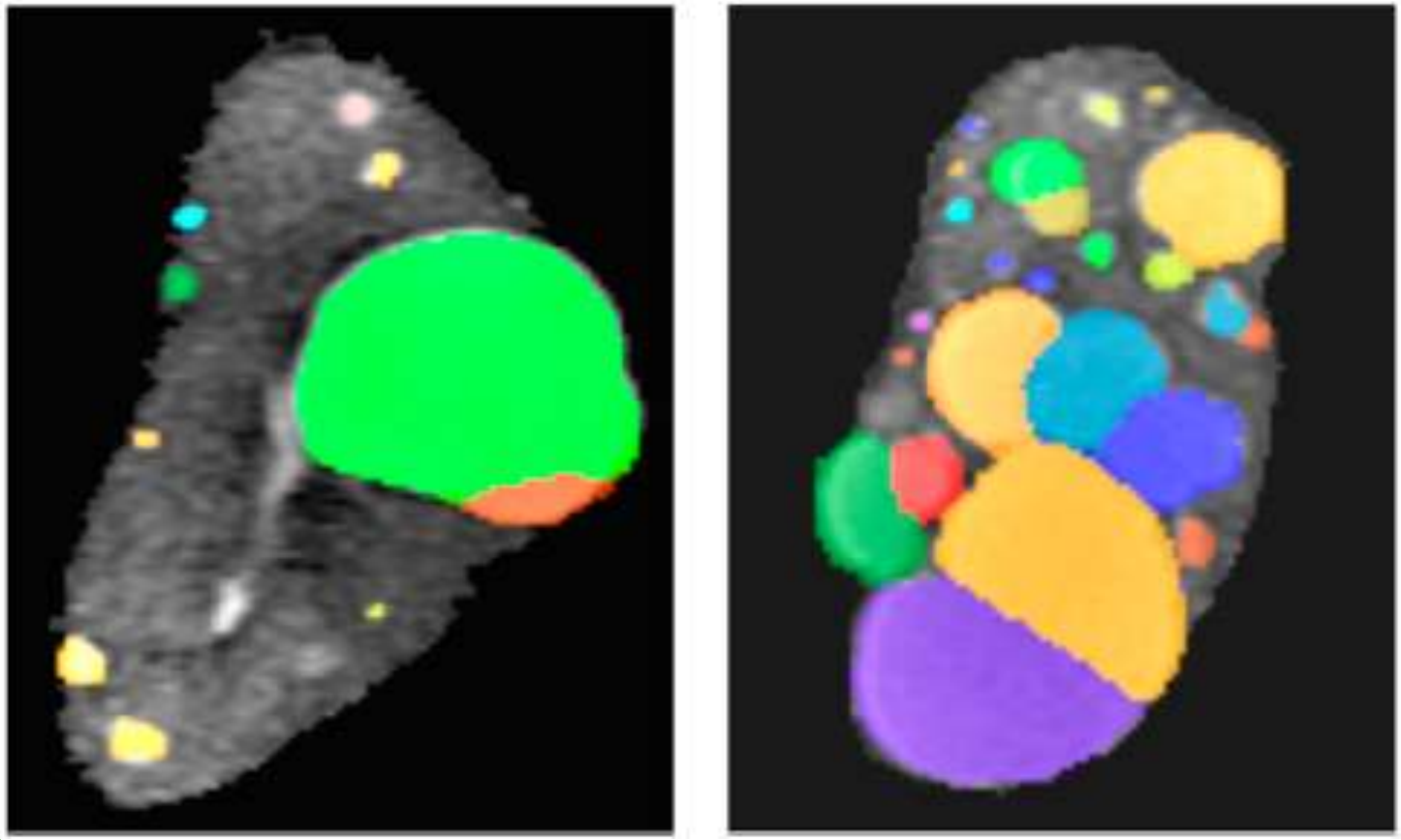
N Engl J Med (2006);354:2122-30.

Which Outcome to Be Considered?



Clin J Am Soc Nephrol (2012)7: 1087–1093.

Segmentation of Individual Renal Cysts



Clin J Am Soc Nephrol (2013); 8: 1089–1097.

PRO

Concept	End Points
Indication: treatment of ADPKD	Primary: Delay in expansion of total kidney volume (biomarker)
Supportive concepts	Secondary
Improvement in symptoms/signs of ADPKD	Symptoms diary (PRO assessment) Signs diary (PRO assessment) Clinical events requiring medical intervention (PRO or non-PRO assessment) Physical exam (non-PRO assessment) Physical performance (PRO or non-PRO assessment)

Am J Kidney Dis. (Dec 2013);62(6):1046-1057

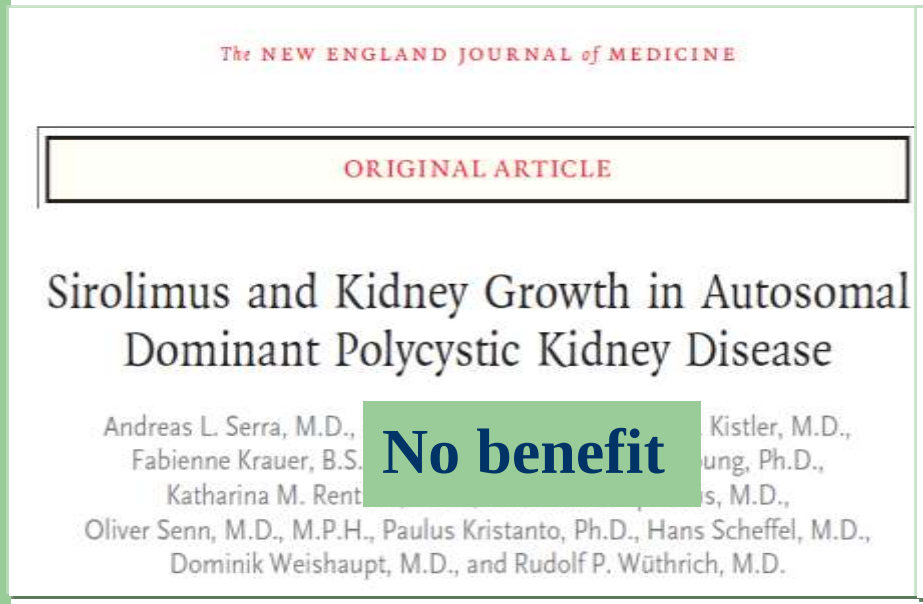
m-TORIs

Effect of mTOR Inhibitors: Preclinical Studies

Drug dose	Model	Duration of treatment	Outcome	Blood levels (ng/mL)	Side effects
Sirolimus 0.2 mg/kg/d IP	Male Han:SPRD	Age 4–8 wk	Decreased kidney enlargement and cyst volume. Improved kidney function.	Not reported	Reduced body weight by 22%
Sirolimus 2 mg/kg/d orally	Male Han:SPRD	3 mo	Decreased kidney enlargement and cyst volume. Improved kidney function.	0.5–1.9	No change in body weight
Everolimus 3 mg/kg/d orally	Male Han:SPRD	5 wk	Decreased kidney enlargement and cyst volume. Improved kidney function.	5–7	Impaired weight gain
Sirolimus 5 mg/kg/d IP	orpk rescue mouse	Age 150–178 d	Decrease in cyst volume.	Not reported	
Sirolimus 5 or 1.67 mg/kg/d IP	bpk mouse	Age 7–21 d	Decrease in cyst volume. Normalization of kidney function.	Not reported	
Sirolimus 0.2 mg/kg/d IP	Male Han:SPRD	Age 1–12 mo	Normalized kidney volume, renal function, blood pressure and heart weight.	6.6–6.9.	Reduced body weight by 11%
Sirolimus 0.2 mg/kg/d IP	Female Han:SPRD rat	Age 4–12 wk	No effect on kidney and cyst volume.	5.9	Reduced body weight by 15%
Sirolimus 5 mg/kg/d IP.	Pkd1 knockout	Age 28–49 d	Reduced cyst growth. Preserved renal function.	Not reported	
Sirolimus 0.5 mg/kg/d IP	Pkd2 knockout	Age 4–16 wk	Reduced kidney size and cyst volume. No effect on kidney function.	22	No change in body weight
Everolimus 3 mg/kg orally	Male Han:SPRD	4–9 wk treatment (pulse). 4–16 wk treatment (continuous).	Both regimens reduced cyst volume and improved kidney function.	4.7–6.2	Impaired weight gain
Sirolimus 2 mg/kg orally	pck rat	4, 8, or 12 wk	No effect on liver and kidney cysts	0.6	Reduced weight gain
Low dose (10 mg/kg) vs. High dose (100 mg/kg) orally	Pkd1 knockout mice	Early vs. late treatment	Low dose did not affect renal cysts. Early treatment was better than late treatment.	3 vs. 30–60	Not reported

Kidney Res Clin Pract 31 (2012) 132–138

Effect of mTOR Inhibitors: Clinical Studies



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

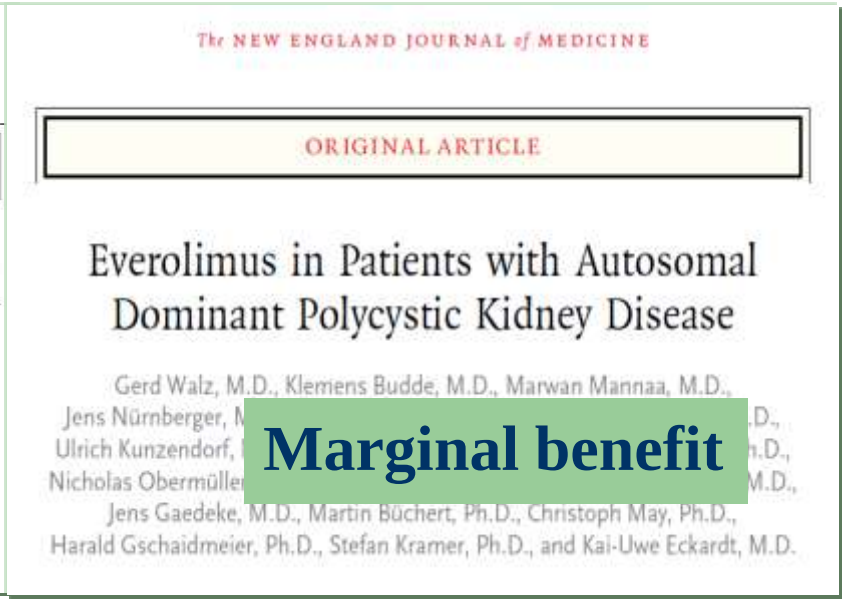
Sirolimus and Kidney Growth in Autosomal Dominant Polycystic Kidney Disease

Andreas L. Serra, M.D., … Kistler, M.D., Fabienne Krauer, B.S. … ung, Ph.D., Katharina M. Rent … s, M.D., Oliver Senn, M.D., M.P.H., Paulus Kristanto, Ph.D., Hans Scheffel, M.D., Dominik Weishaupt, M.D., and Rudolf P. Wüthrich, M.D.

No benefit

100 patients
Open label RT
2mg/stand (18m)

N Engl J Med (2010);363:820-9.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Everolimus in Patients with Autosomal Dominant Polycystic Kidney Disease

Gerd Walz, M.D., Klemens Budde, M.D., Marwan Mannaa, M.D., Jens Nürnberger, M… D., Ulrich Kunzendorf, … h.D., Nicholas Obermüller… M.D., Jens Gaedeke, M.D., Martin Büchert, Ph.D., Christoph May, Ph.D., Harald Gschaidmeier, Ph.D., Stefan Kramer, Ph.D., and Kai-Uwe Eckardt, M.D.

Marginal benefit

433 patients
Double blind RT
24 m

N Engl J Med (2010);363:830-40.

Effect of mTOR Inhibitors:
Metanalysis (5RCT; n=619 P)

- Long-term treatment with TORIs does not benefit patients with ADPKD.

Nephron Clin Pract.(2013 Sep 6);124(1-2):10-16

Effect of mTOR Inhibitors: From Bench to Bedside

ELSEVIER

Kidney Research and Clinical Practice

journal homepage: http://www.krcp-ksn.com
Contents lists available at ScienceDirect

Review Article

Mammalian target of rapamycin inhibition in polycystic kidney disease: From bench to bedside

Why the human studies are unimpressive?

What will be needed in the clinical studies?

Kidney Res Clin Pract 31 (2012) 132–138

Dose-Dependent Effects of Sirolimus

BASIC RESEARCH www.jasn.org

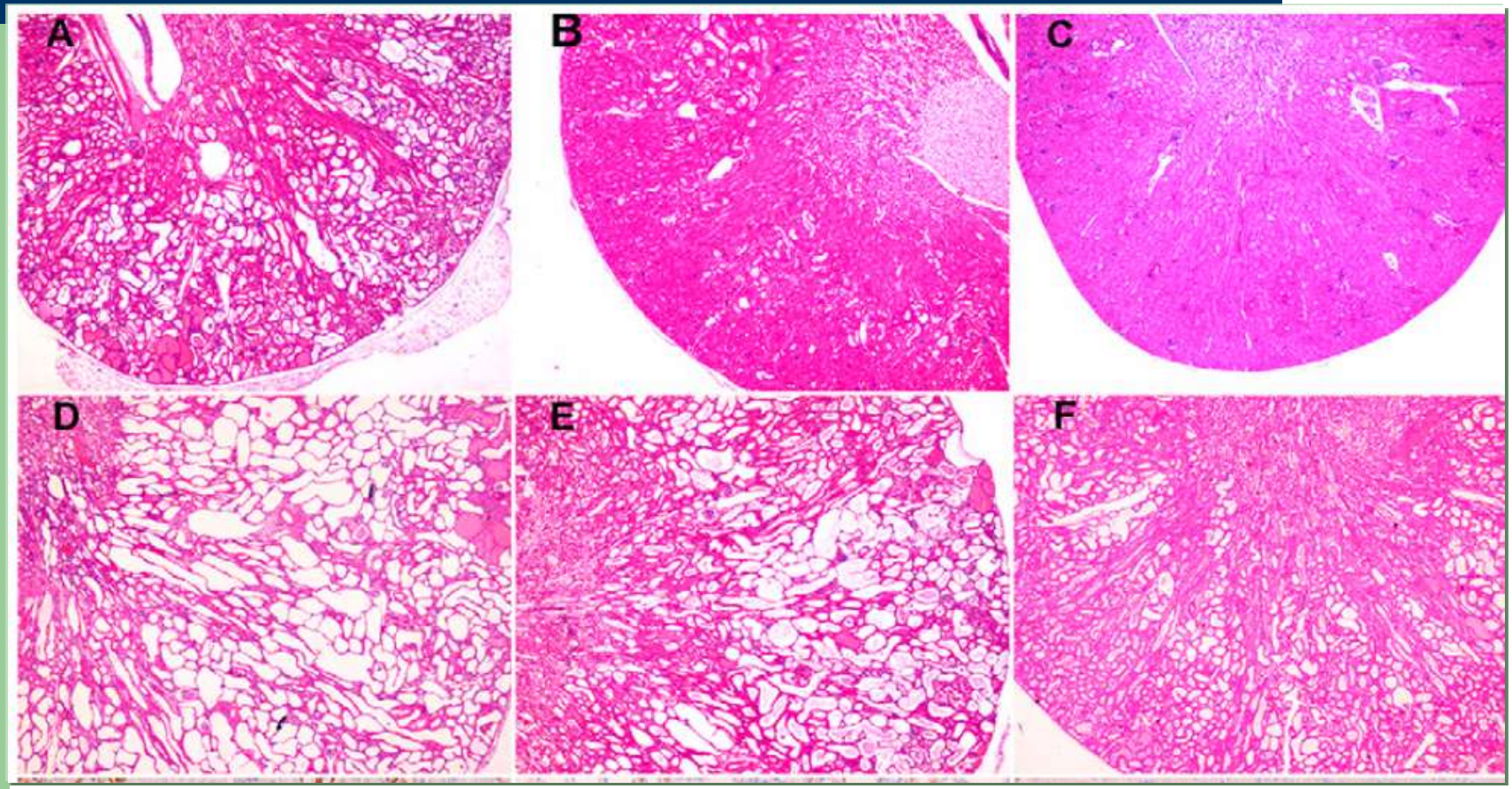
Dose-Dependent Effects of Sirolimus on mTOR Signaling and Polycystic Kidney Disease

Zlata Novalic,* Annemieke M. van der Wal,† Wouter N. Leonhard,* Gudrun Koehl,‡ Martijn H. Breuning,* Edward K. Geissler,‡ Emile de Heer,† and Dorien J.M. Peters*

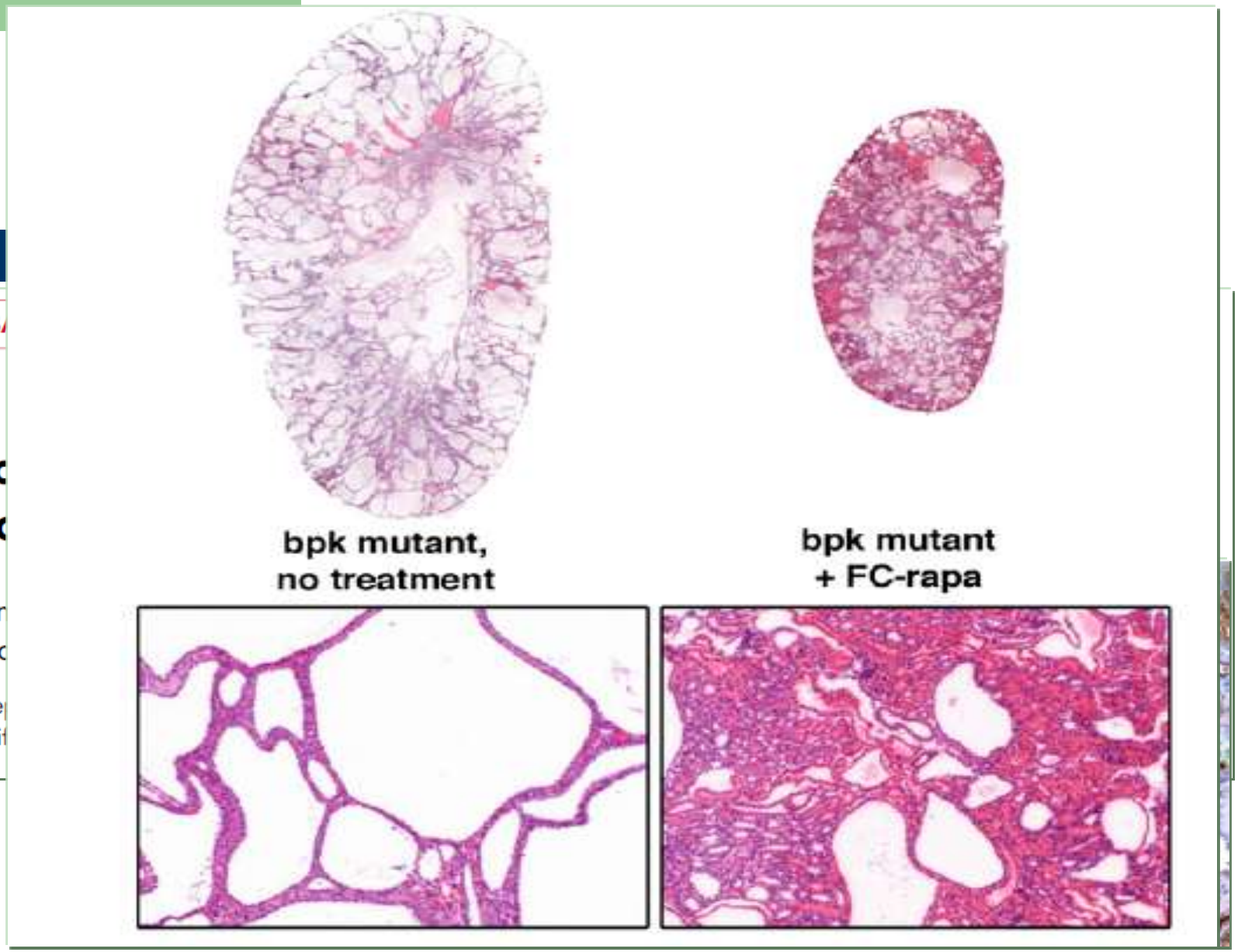
*Departments of Human and Clinical Genetics and †Pathology, Leiden University Medical Center, Leiden, The Netherlands; and ‡Department of Surgery, University Hospital Regensburg, University of Regensburg, Regensburg, Germany

J Am Soc Nephrol (2012) 23: 842–853.

Dose-Dependent Effects of Sirolimus



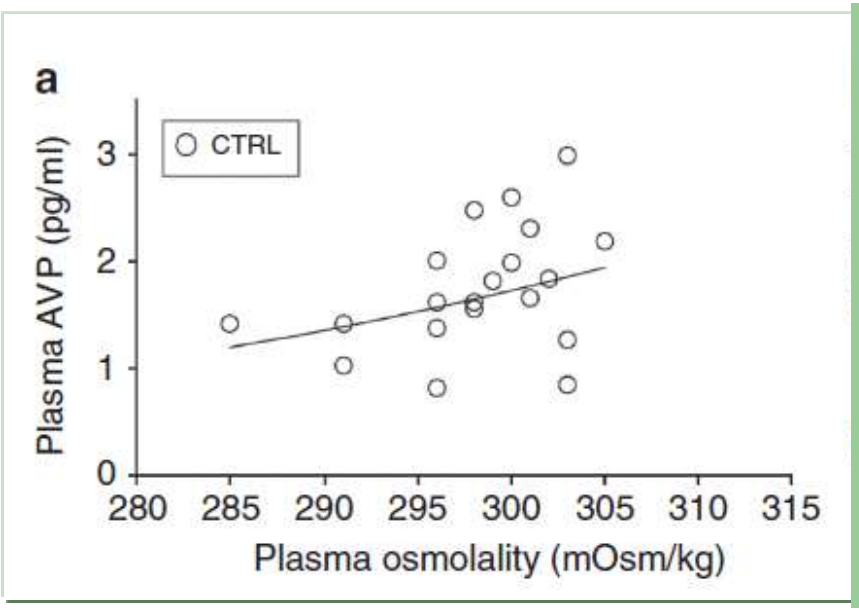
J Am Soc Nephrol (2012) 23: 842–853.



J Am Soc Nephrol (2012) 23: 1674–1681.

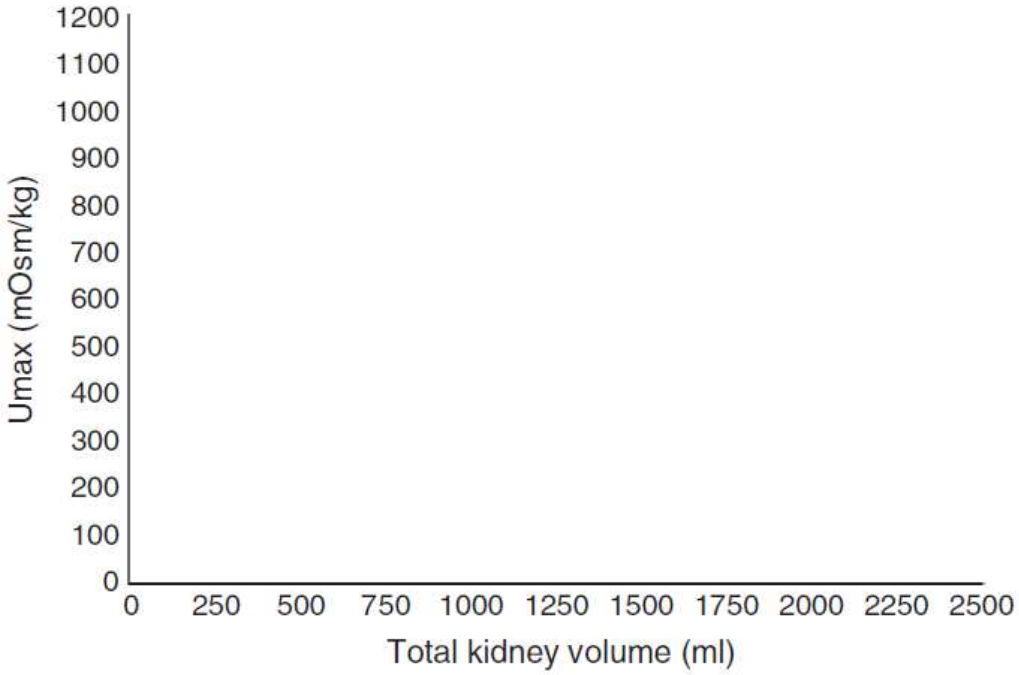
Vasopressin pathway

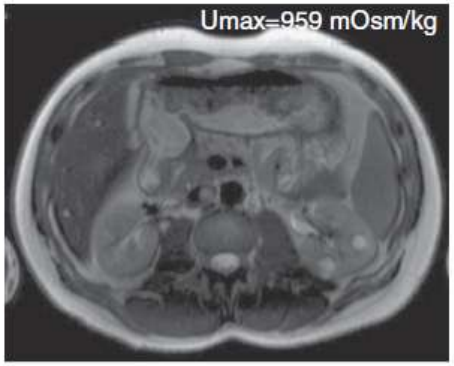
Plasma Osmolality and AVP

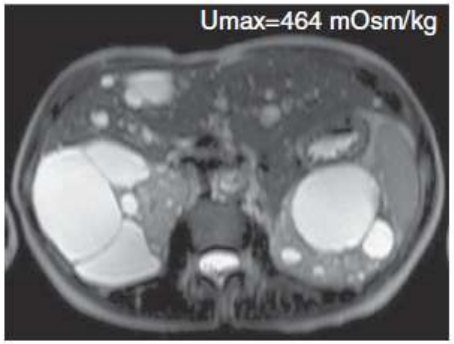


Kidney International (2012) 82, 1121–1129

Urine Osmolality in ADPCK

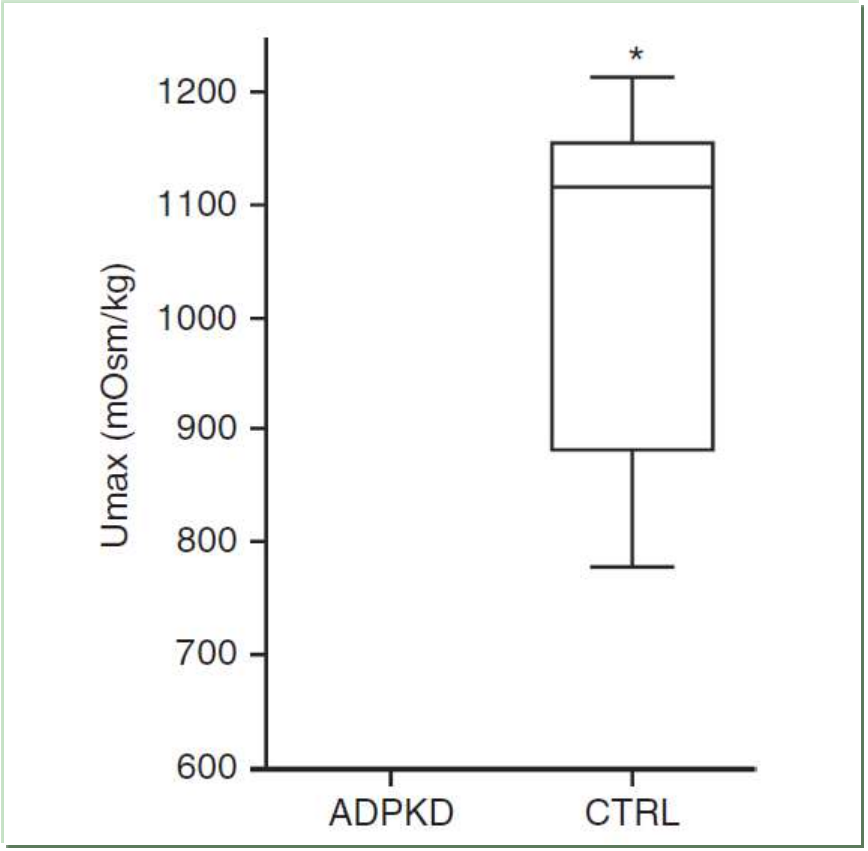






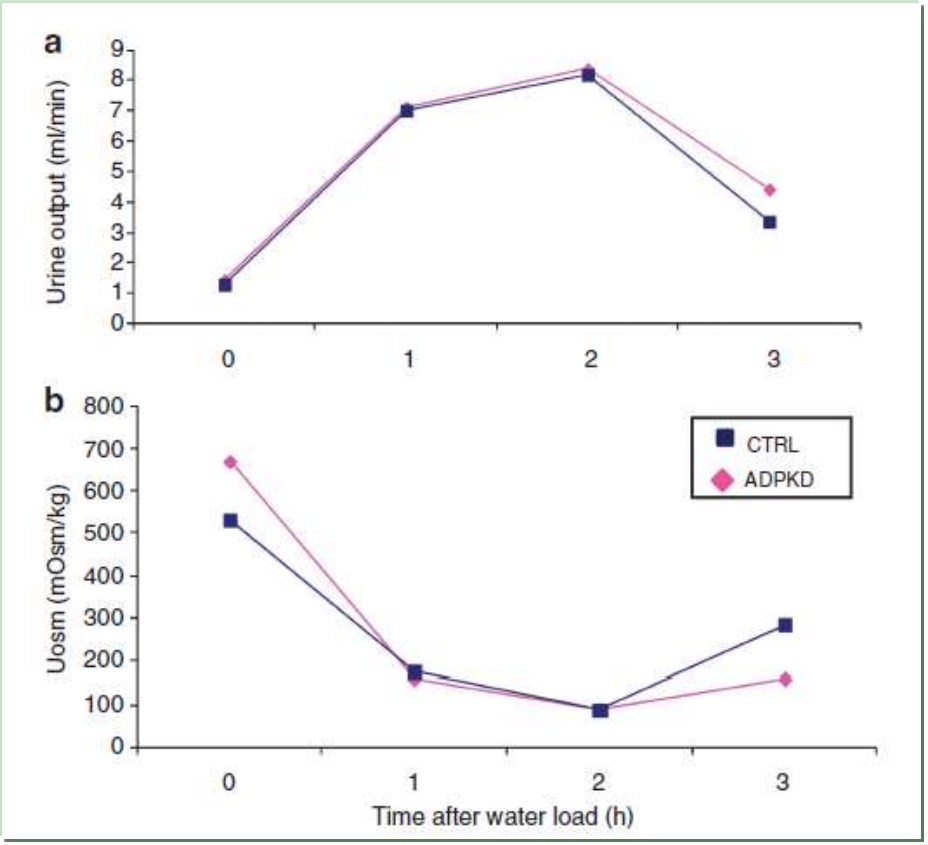
Kidney International (2012) 82, 1121–1129

Urine Osmolality After Overnight Water Deprivation



Kidney International (2012) 82, 1121–1129

Response to Acute Water Loading



Kidney International (2012) 82, 1121–1129

http://www.kidney-international.org review

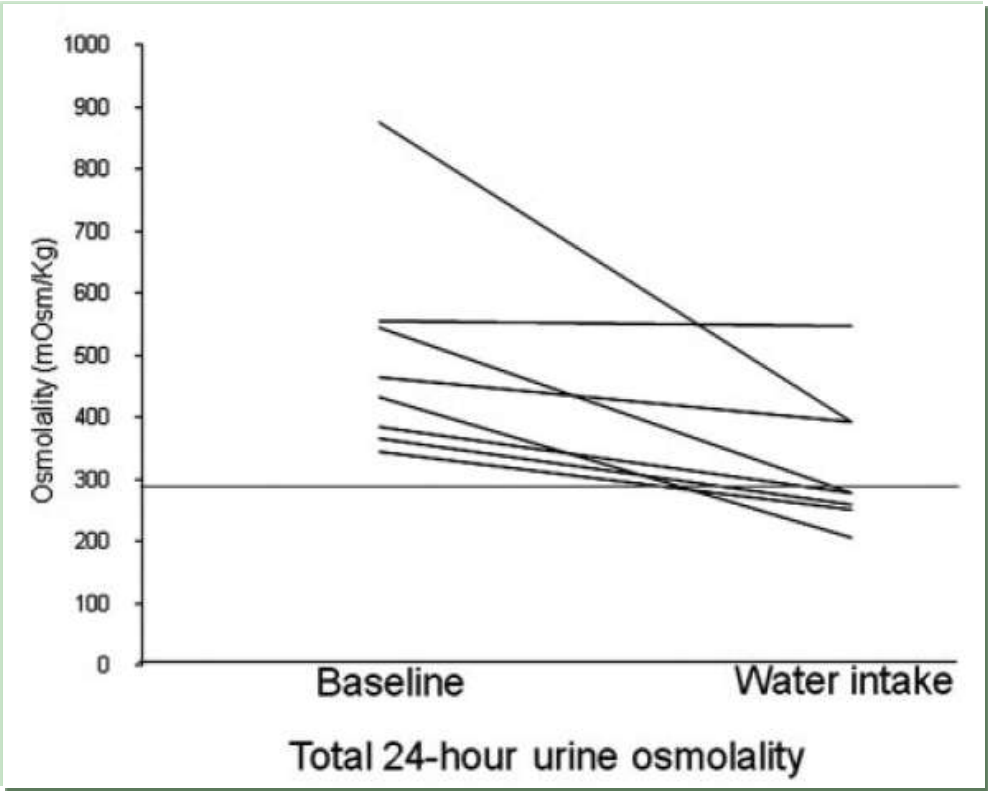
The medicinal use of water in renal disease

Connie J. Wang[1], Jared J. Grantham[1] and James B. Wetmore[1]

[1]*Division of Nephrology and the Kidney Institute, University of Kansas Medical Center, Kansas City, Kansas, USA*

Water Prescription in ADPCK

$$\frac{\text{Total solutes (mosmol)}}{\text{285 (mosm/kg)}} - \text{Volume (ml)}$$



Clin J Am Soc Nephrol (2011) 6: 192–197.

Water Prescription in ADPCK

GFR ≥ 60 ml/min/1.73 m^2	60 > GFR > 30 ml/min/1.73 m^2	GFR ≤ 30 ml/min/ 1.73 m^2

Exclusions:

1. Severe protein or sodium restriction
2. Volume contraction or reduced effective IVV
3. Diuretics or drugs enhancing the release or effect of AVP
4. Abnormal voiding mechanisms

Clin J Am Soc Nephrol (2009); 4: 1140–1150.

Water Prescription in ADPCK: n: 17/13

Original Articles

Does increased water intake prevent disease progression in autosomal dominant polycystic kidney disease?

	High water-intake group	Free water-intake group	P value
Primary end point (kidney volume slope)			
TKV slope (mL/year)	163 ± 124	99 ± 118	0.13
% TKV slope (%/year)	9.68 ± 6.64	5.28 ± 7.70	0.083
Ht-TKV slope (mL/m/year)	99.5 ± 75.1	61.4 ± 76.2	0.15
Secondary end point (kidney function slope)			
Ccr slope (mL/min/1.73 m^2/year)	−15.4 ± 34.0	−2.6 ± 19.2	0.19
eGFR ($Eq_{cr\text{-}cys}$) slope (mL/min/1.73 m^2/year)	−5.6 ± 6.5	−1.1 ± 7.0	0.059
eGFR (Eq_{cr}) slope (mL/min/1.73 m^2/year)	−7.1 ± 8.6	−2.7 ± 7.3	0.12
Secondary end point (AVP and copeptin)			
Plasma AVP (pg/mL)	2.7 ± 2.4	5.2 ± 3.6	0.024
Plasma copeptin (pmol/L)	7.6 ± 4.0	14.4 ± 10.5	0.016
Secondary end point (QOL)			
How many times did you void during daytime?	8.6 ± 1.6	6.5 ± 1.3	<0.001
How many times did you void at night?	0.8 ± 0.6	0.5 ± 0.4	0.10
How problematic is daytime frequency?[a]	2.5 ± 0.9	1.8 ± 1.1	0.069
How problematic is nocturnal frequency?[a]	2.3 ± 1.0	1.6 ± 1.0	0.070

Nephrol Dial Transplant (2014) 29: 1710–1719

TEMPO

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease

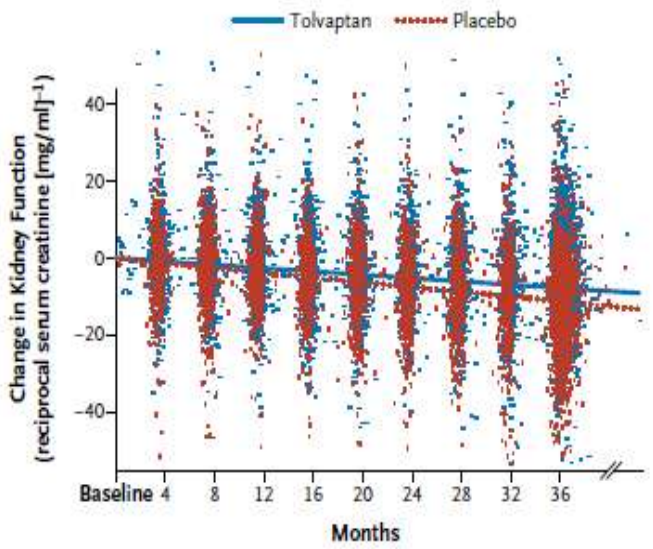
Double blind placebo RCT
1445 patients: 2:1 ratio to receive tolvaptan

Tolvaptan Efficacy and Safety in Management of ADPCKD and Its Outcomes

N Engl J Med (2012);367:2407-18.

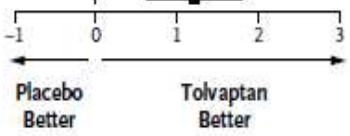
TEMPO

C Kidney Function



D Treatment Effect for Kidney Function

Subgroup	Absolute Treatment Effect: Difference in annual slope ([mg/ml]$^{-1}$)	Relative Treatment Effect: %	Annual Slope: Tolvaptan (mg/ml)$^{-1}$	Annual Slope: Placebo (mg/ml)$^{-1}$	P Value
Sex					
Male		32.1	−2.37	−3.49	<0.001
Female		30.7	−2.85	−4.11	0.02
Age					
<35 yr		26.5	−1.93	−2.62	0.19
≥35 yr		30.6	−2.84	−4.09	<0.001
Hypertension					
Yes		35.0	−2.72	−4.19	<0.001
No		9.6	−2.09	−2.31	0.69
Estimated creatinine clearance					
<80 ml/min		32.0	−3.69	−5.43	0.01
≥80 ml/min		29.7	−2.21	−3.14	0.001
Total kidney volume					
<1500 ml		21.7	−1.97	−2.52	0.10
≥1500 ml		36.6	−3.24	−5.11	<0.001
All patients		31.6	−2.61	−3.81	<0.001

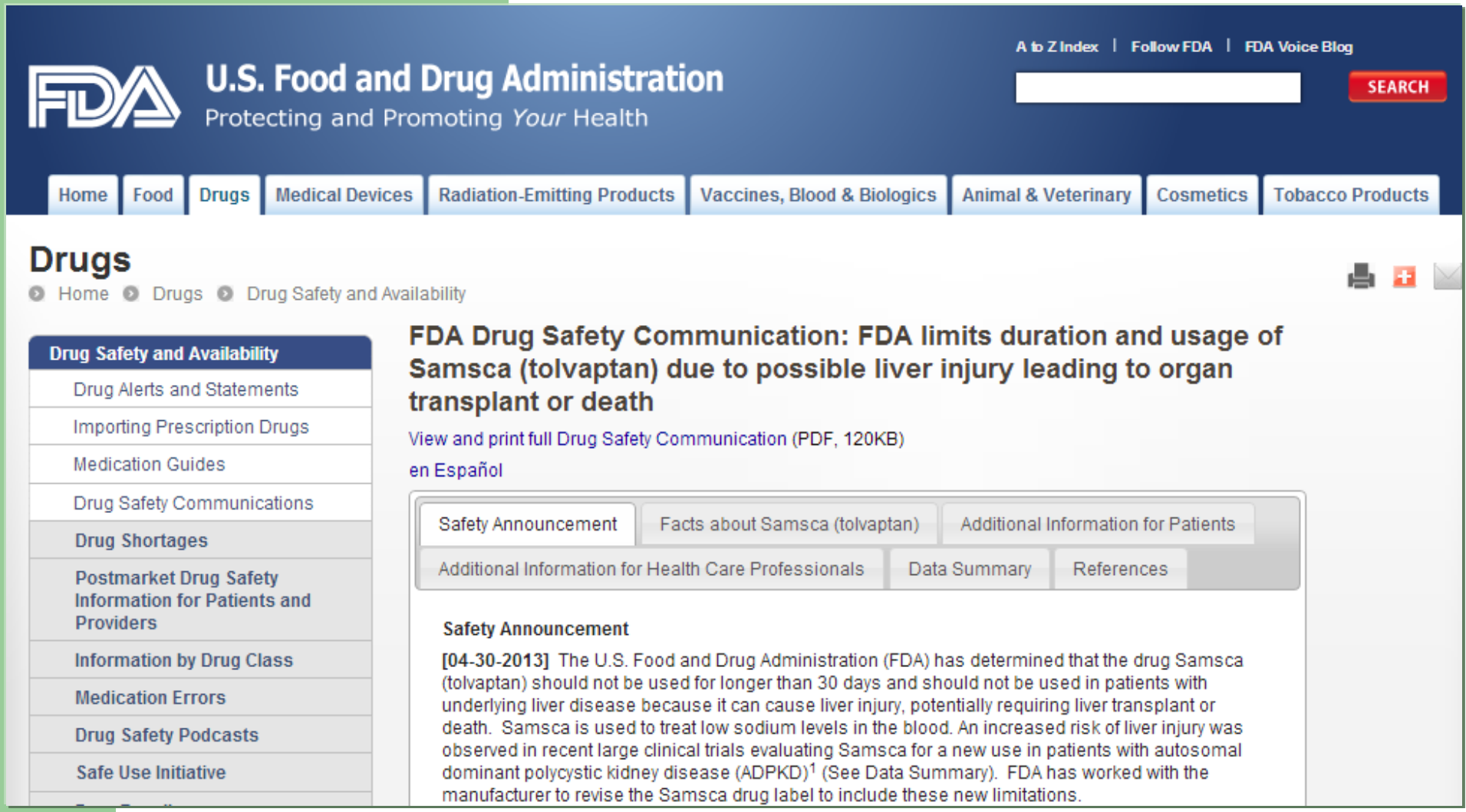


N Engl J Med (2012);367:2407-18.

TEMPO

Event	Tolvaptan (N=961)	Placebo (N=483)
Discontinuation rate	**23%**	**14%**
Serious adverse events more common in tolvaptan group		
Alanine aminotransferase elevation	9 (0.9)	2 (0.4)
Aspartate aminotransferase elevation	9 (0.9)	2 (0.4)
Chest pain	8 (0.8)	2 (0.4)
Headache	5 (0.5)	0

N Engl J Med (2012);367:2407-18.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Drug Shortages
Postmarket Drug Safety Information for Patients and Providers
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Medication Errors
Drug Safety Podcasts
Safe Use Initiative
FDA Drug Safety Communication: FDA limits duration and usage of Samsca (tolvaptan) due to possible liver injury leading to organ transplant or death
View and print full Drug Safety Communication (PDF, 120KB)
en Español
Safety Announcement
Facts about Samsca (tolvaptan)
Additional Information for Patients
Additional Information for Health Care Professionals
Data Summary
References
Safety Announcement
[04-30-2013] The U.S. Food and Drug Administration (FDA) has determined that the drug Samsca (tolvaptan) should not be used for longer than 30 days and should not be used in patients with underlying liver disease because it can cause liver injury, potentially requiring liver transplant or death. Samsca is used to treat low sodium levels in the blood. An increased risk of liver injury was observed in recent large clinical trials evaluating Samsca for a new use in patients with autosomal dominant polycystic kidney disease (ADPKD)[1] (See Data Summary). FDA has worked with the manufacturer to revise the Samsca drug label to include these new limitations.

Am J Kidney Dis. 2015 Jan 15. pii: S0272-6386(14)01465-6. doi: 10.1053/j.ajkd.2014.11.010. [Epub ahead of print]

Short-term Effects of Tolvaptan in Individuals With Autosomal Dominant Polycystic Kidney Disease at Various Levels of Kidney Function.

NDT Advance Access published February

Nephrol Dial Transplant (2014) 0: 1–39
doi: 10.1093/ndt/gfu040

Clinical Practice Guideline

Clinical practice guideline on diagnosis and treatment of hyponatraemia

7.4.3.1. In moderate or profound hyponatraemia, we suggest restricting fluid intake as first-line treatment (2D).

7.4.3.2. In moderate or profound hyponatraemia, we suggest the following can be considered equal second-line treatments: increasing solute intake with 0.25–0.50 g/kg per day of urea or a combination of low-dose loop diuretics and oral sodium chloride (2D).

7.4.3.3. In moderate or profound hyponatraemia, we recommend against lithium or demeclocycline (1D).

7.4.3.4. In moderate hyponatraemia, we do not recommend vasopressin receptor antagonists (1C).

7.4.3.5. In profound hyponatraemia, we recommend against vasopressin receptor antagonists (1C).

Long acting somatostatin analogue

Effect of Long-Acting Somatostatin Analogue

CLINICAL RESEARCH www.jasn.org

Randomized Clinical Trial of Long-Acting Somatostatin for Autosomal Dominant Polycystic Kidney and Liver Disease

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J Am Soc Nephrol (2010) ;21: 1052–1061.

Effect of Long-Acting Somatostatin Analogue

	Octreotide-LAR			Placebo			p value
	Baseline (n=38)	1 year (n=38)	3 year (n=35)	Baseline (n=37)	1 year (n=37)	3 year (n=35)	
TKV							
Mean (mL)	1556·9 (167·9)	1603·1 (176·1)	1672·7 (202·0)	2161·2 (209·6)	2304·9 (224·6)	2621·0 (271·0)	..
Absolute change (mL)	..	46·2 (18·2)	220·1 (49·1)	..	143·7 (26·0)	454·3 (80·8)	0·032*; 0·25†
Annual slope (mL per year)	..	..	76·6 (16·8)	..	..	152·0 (27·4)	0·0085
HtTKV							
Mean (mL/m)	905·8 (92·1)	932·3 (96·7)	970·1 (109·2)	1266·7 (120·7)	1350·4 (128·8)	1535·2 (156·0)	..
Absolute change (mL/m)	..	26·4 (10·3)	125·5 (27·8)	..	83·6 (14·9)	264·9 (47·1)	0·030*; 0·23†
Annual slope (mL/m per year)	..	..	43·7 (9·5)	..	..	88·6 (16·0)	0·0078
TCV							
Mean (mL)	1073·2 (141·0)	1078·02 (146·9)	1136·4 (166·6)	1513·9 (168·5)	1591·4 (179·4)	1876·5 (218·5)	..
Absolute change (mL)	..	33·0 (14·7)	183·8 (41·7)	..	108·5 (18·3)	394·7 (62·9)	0·017*; 0·11†
Annual slope (mL per year)	..	..	64·4 (14·3)	..	..	133·2 (21·4)	0·0076
NCV							
Mean (mL)	546·7 (38·4)	556·7 (38·6)	571·1 (45·7)	679·8 (54·9)	713·5 (58·0)	744·5 (67·1)	..
Absolute change (mL)	..	13·4 (10·2)	45·0 (14·6)	..	35·0 (13·7)	67·1 (36·3)	0·34*; 0·71†
Annual slope (mL per year)	..	..	15·4 (4·7)	..	..	21·5 (12·4)	0·12

Data are mean (SE). Annual slopes compared by Wilcoxon rank sum test. All other comparisons performed by ANCOVA adjusting for baseline value. LAR=long-acting release. TKV=total kidney volume. HtTKV=height adjusted TKV. TCV=total cyst volume. NCV=non-cyst volume. *Octreotide-LAR versus placebo at 1 year. †Octreotide-LAR versus placebo at 3 years.

Lancet (November 2013); 382: 1485–95

Effect of Long-Acting Somatostatin Analogue

mGFR (iohexol plasma clearance technique)

	Octreotide-LAR				Placebo			
	Baseline (n=36)	1 year (n=34)	2 year (n=34)	3 year (n=36)	Baseline (n=34)	1 year (n=32)	2 year (n=33)	3 year (n=31)
Mean (mL/min per 1·73m²)	88·68 (3·93)	77·86 (4·23)	78·50 (4·82)	76·33 (4·66)	77·77 (5·30)	72·16 (5·45)	67·98 (6·28)	64·64 (6·51)
Annual slope (mL/min per 1·73m² per year)								
0–3 years	..	..	..	−3·85* (−6·20 to −1·92)	..	..	..	−4·95 (−7·49 to −1·97)
1–3 years	..	..	..	−2·28† (−5·34 to 0·43)	..	..	..	−4·32 (−7·77 to −1·19)

Data are mean (SE) or median (IQR). LAR=long-acting release. *Wilcoxon rank sum test p versus placebo=0·13. †Wilcoxon rank sum test p versus placebo=0·027.

Lancet (November 2013); 382: 1485–95

Effect of Long-Acting Somatostatin Analogue

	Octreotide-LAR (n=40)	Placebo (n=39)
Overall	6 (15·0%)	7 (18·0%)
Sepsis	1 (2·5%)	2 (5·1%)
Cholelithiasis	2 (5·0%)	0
Acute cholecystitis	2 (5·0%)	0
Gastroenteritis	0	1 (2·6%)
Hepatitis C	0	1 (2·6%)
Haemorrhagic hepatic cyst	1 (2·5%)	0
Nephrolithiasis	0	1 (2·6%)
Renal cyst haemorrhage	1 (2·5%)	1 (2·6%)
Urinary tract infection	2 (5·0%)	1 (2·6%)
Intracranial aneurysm	1 (2·5%)	0
Hypertensive crisis	0	1 (2·6%)
Acute worsening of chronic renal dysfunction	0	1 (2·6%)
Spinal column injury	0	1 (2·6%)

Data are n (%). Excludes one foot fracture and one pregnancy in the octreotide-LAR group. LAR=long-acting release.

Lancet (November 2013); 382: 1485–95

Anti-Hypertensive Drugs

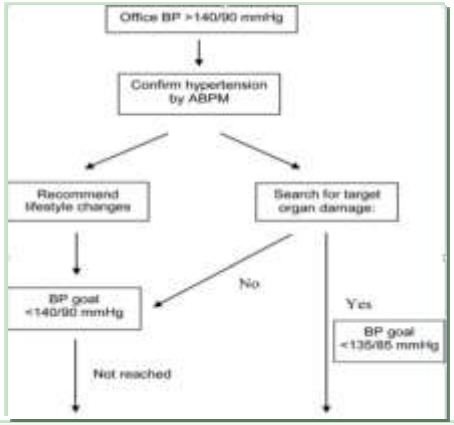
Hypertension in ADPCK

Potential pathophysiological mechanisms of hypertension and cardiovascular risk in early ADPKD

(i) Cyst growth and renal enlargement
(ii) Renal ischaemia/hypoxia
(iii) Increased in erythropoietin
(iv) Activation RAAS
(v) Increased in vasopressin and cAMP
(vi) Vascular dysfunction
(vii) Decreased nitric oxide production
(viii) Cardiac and valvular disorders

Clin Kidney J (October 2013) 6: 457–463

Hypertension in ADPCK



Pharmacological treatment:
1st step: RAAS inhibitors
2nd step: RAAS inhibitors + beta-blockers
3rd step: RAAS inhibitors + beta-blockers + diuretic (and consider CCB as 4th step treatment)

Clin Kidney J (October 2013) 6: 457–463

What is BP Goal in ADPCK?

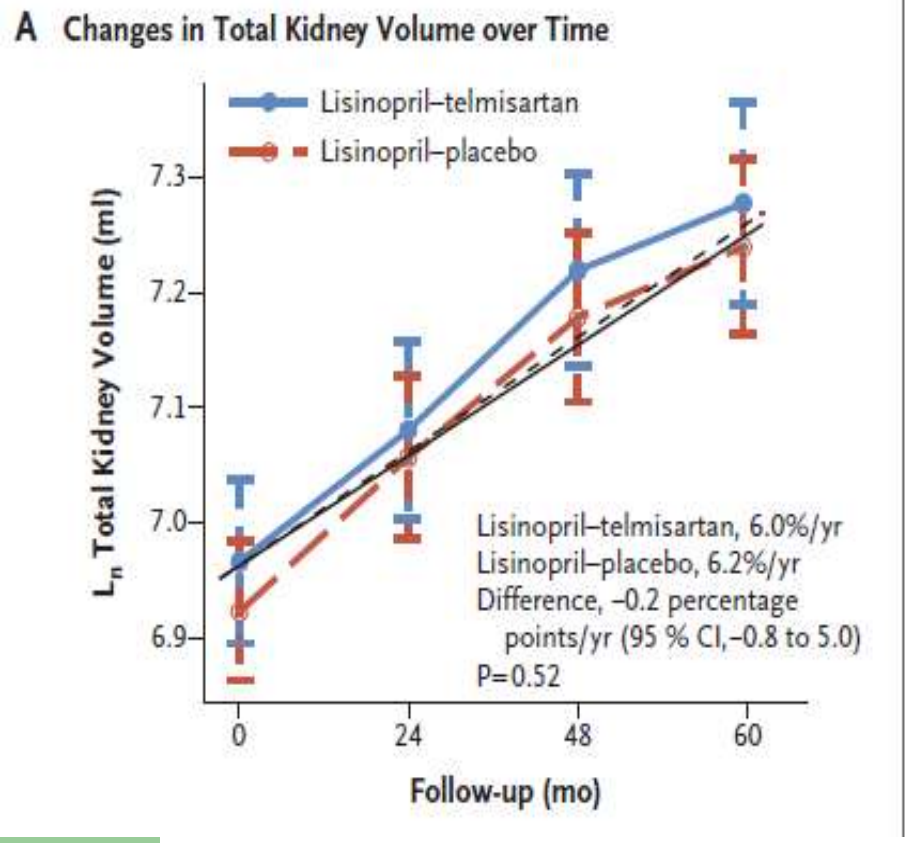
- Less than 140/90 in all cases
- Less than 135/85 as soon as microalbuminuria or LVH is present

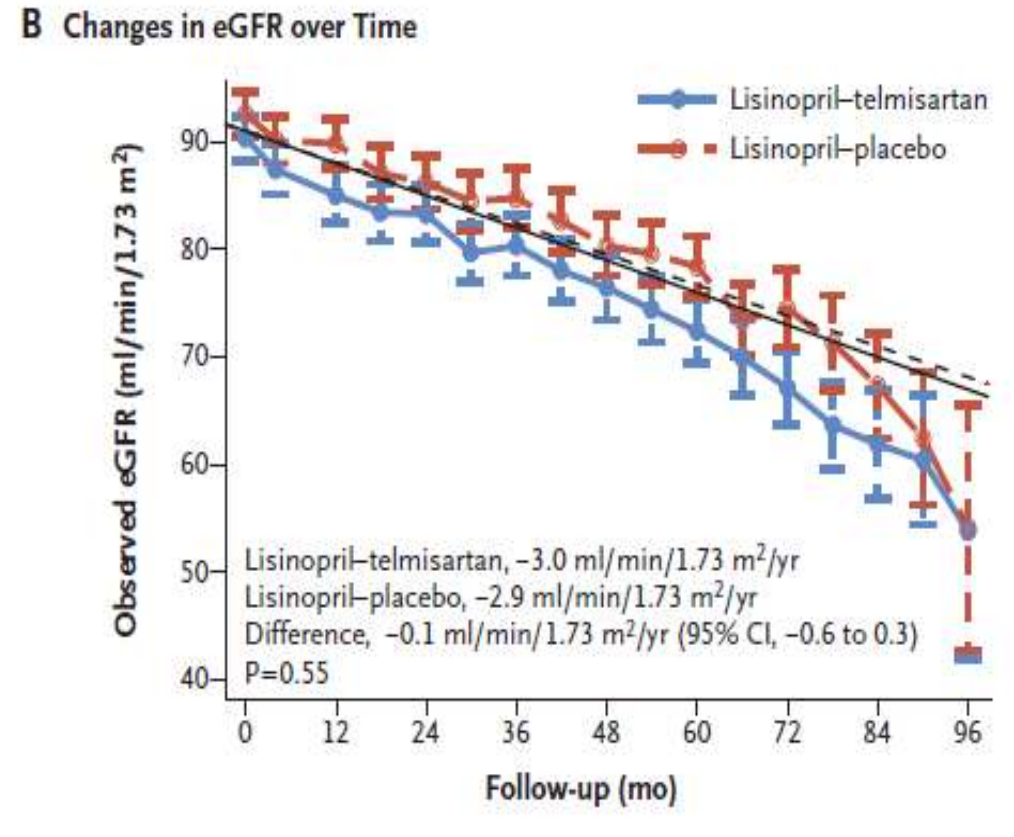
Design of HALT PKD Trials

	STUDY A	STUDY B
Study B		
1–4	Combination ACEi/ARB Lisinopril 5 mg/Telmisartan 40 mg Lisinopril 10 mg/Telmisartan 40 mg Lisinopril 20 mg/Telmisartan 80 mg Lisinopril 40 mg/Telmisartan 80 mg	Combination ACEi/Placebo Lisinopril 5 mg/Placebo 40 mg Lisinopril 10 mg/Placebo 40 mg Lisinopril 20 mg/Placebo 80 mg Lisinopril 40 mg/Placebo 80 mg
5 and 6	Furosemide 20 mg BID Furosemide 40 mg BID	Furosemide 20 mg BID Furosemide 40 mg BID
7–9	Metoprolol 50 mg BID Metoprolol 100 mg BID Metoprolol 200 mg BID	Metoprolol 50 mg BID Metoprolol 100 mg BID Metoprolol 200 mg BID
≥10	Nondihydropyridine calcium channel blockers (diltiazem), clonidine, minoxidil, hydralazine at discretion of investigator	Nondihydropyridine calcium channel blockers (diltiazem), minoxidil, clonidine, hydralazine at discretion of investigator
	Pressure (≤110/75 vs ≤130/80 mm Hg) and ACEi/ARB vs ACEi/placebo	ACEi/ARB vs ACEi/placebo and Blood Pressure ≤ 130/80 mm Hg

Clin J Am Soc Nephrol (2010);5: 102–109.

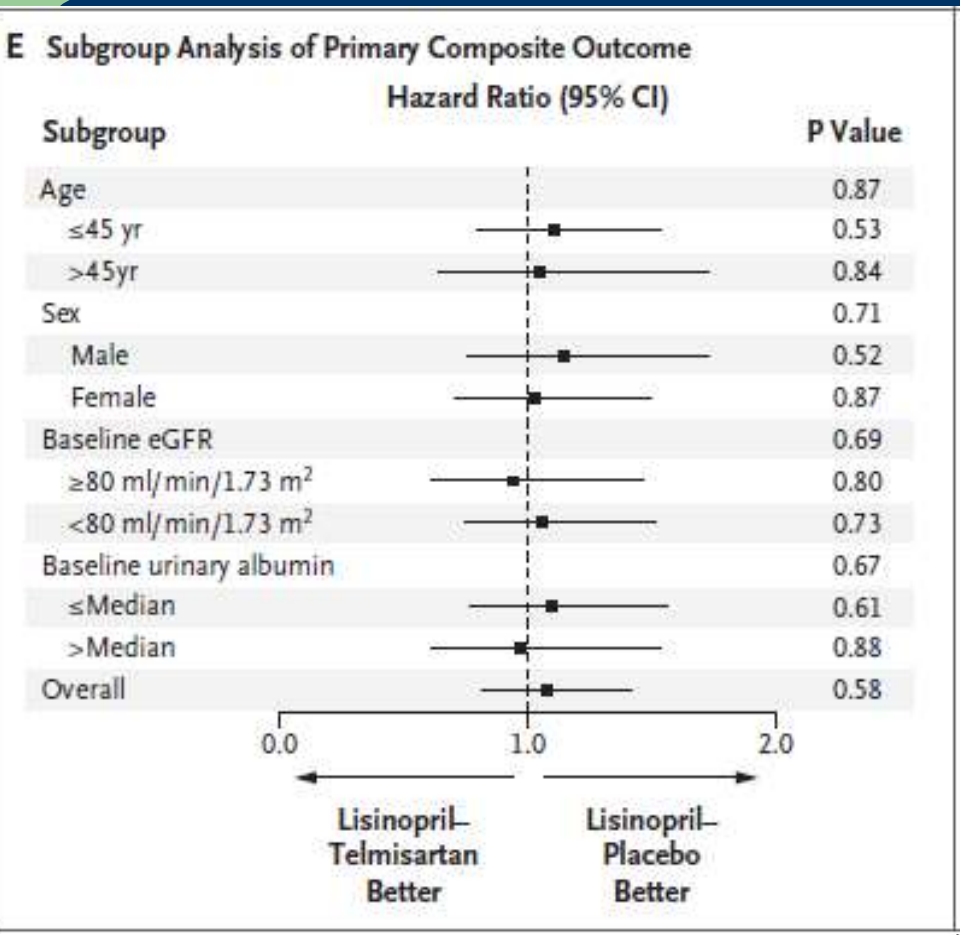
HALT PKD Trials:
Study A

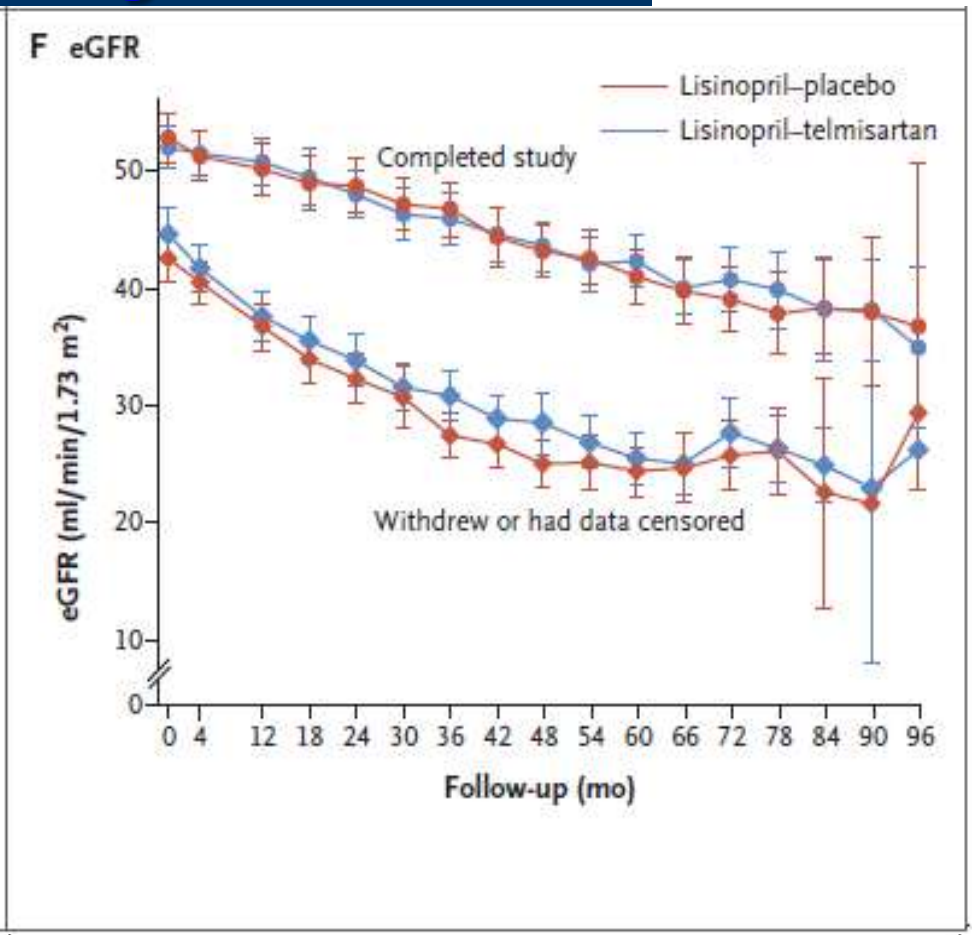




This article was published on November 15, 2014, at NEJM.org.

HALT PKD Trials:
Study B

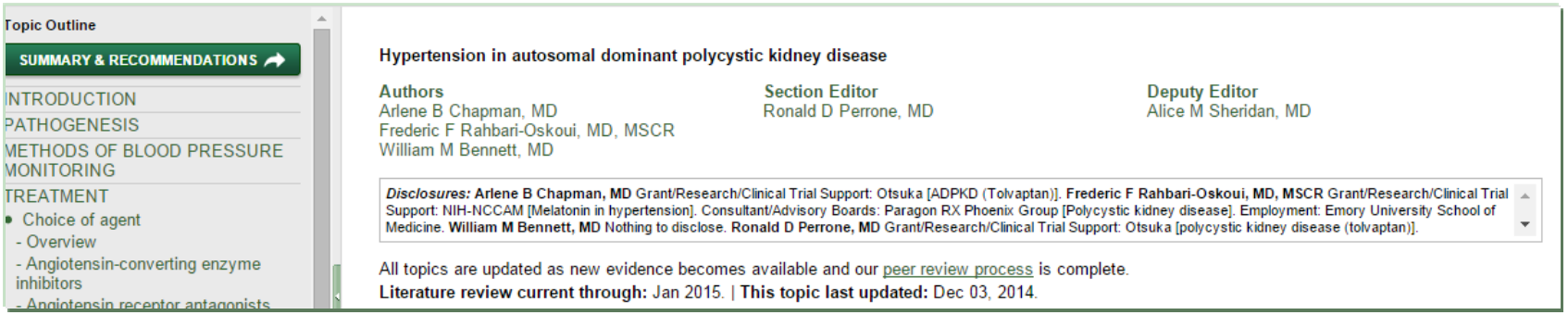




This article was published on November 15, 2014, at NEJM.org.

All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Jan 2015. | **This topic last updated:** Nov 20, 2014.

We do not agree with the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for blood pressure management or with recommendations of the Joint National Committee (JNC)-8 [36] that the optimal target blood pressure is <140/90 mmHg for all CKD patients who do not have proteinuria (including moderately increased albuminuria [formerly called "microalbuminuria"]), which includes many ADPKD patients.



Topic Outline

SUMMARY & RECOMMENDATIONS

INTRODUCTION

PATHOGENESIS

METHODS OF BLOOD PRESSURE MONITORING

TREATMENT

- Choice of agent
  - Overview
  - Angiotensin-converting enzyme inhibitors
  - Angiotensin receptor antagonists

Hypertension in autosomal dominant polycystic kidney disease

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All topics are updated as new evidence becomes available and our peer review process is complete.
Literature review current through: Jan 2015. | **This topic last updated:** Dec 03, 2014.

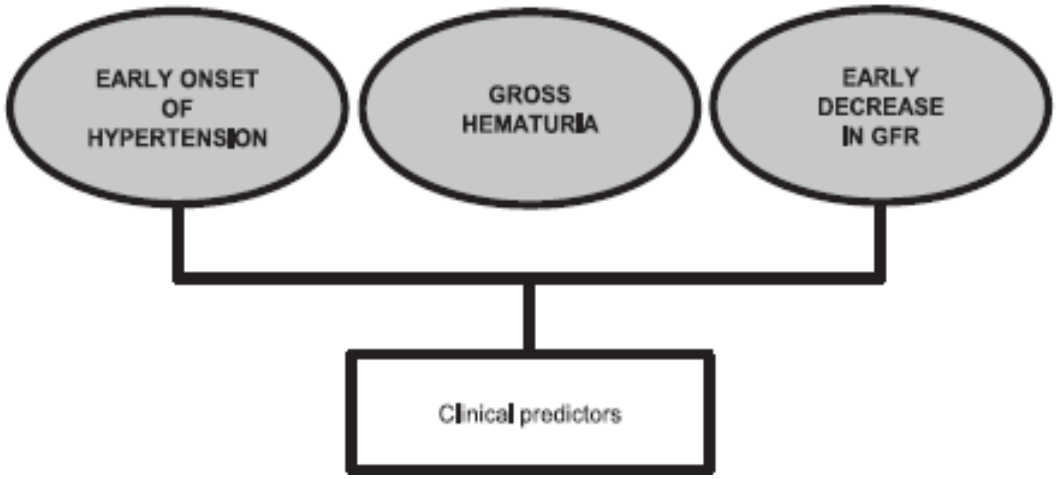
PKD Progression:
Systematic Review

Summary of systematic review process

Step	Procedure	Result
1	Systematic literature review through Medline, EMBASE, and Biosis for articles published from January of 1988 to May of 2013	2056 citations
2	Review abstracts; omit articles not dealing with factors affecting ADPKD severity or progression, reviews, case reports, editorials, commentaries, and letters	1078 citations
3	Omit non-English language articles and articles with focus on transplantation, dialysis, or diabetes, with ESRD used as a cutoff for inclusion	863 citations
4	Omit duplicate references; results separated into four categories: randomized clinical trials; other clinical trials; observational, retrospective, or epidemiologic studies; and preclinical studies	666 articles ranked for inclusion

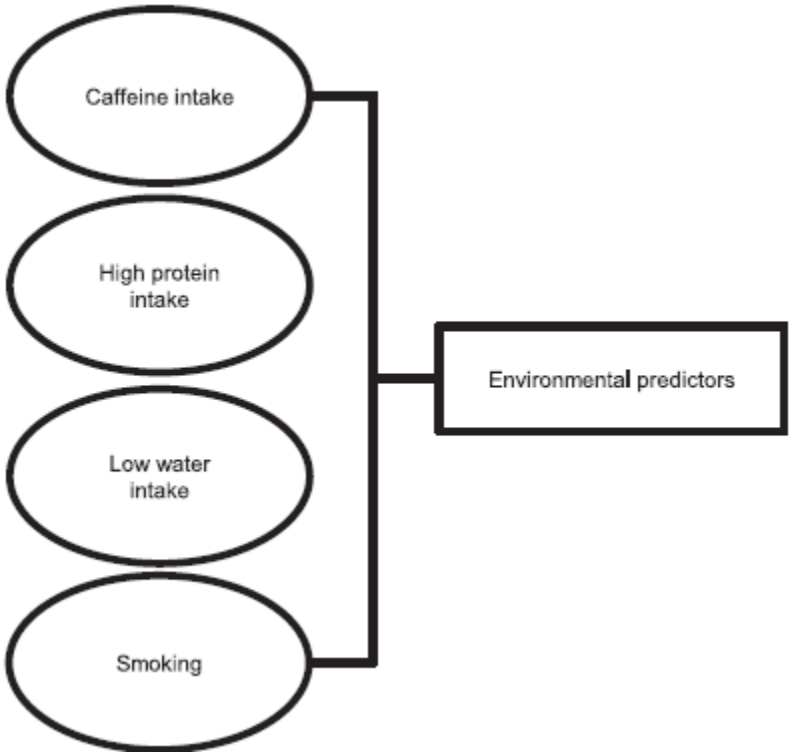
J Am Soc Nephrol 25: 2399–2418, November 2014.

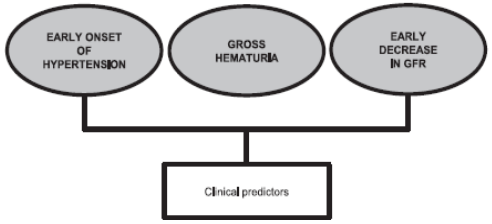
PKD Progression:
Systematic Review



J Am Soc Nephrol 25: 2399–2418, November 2014.

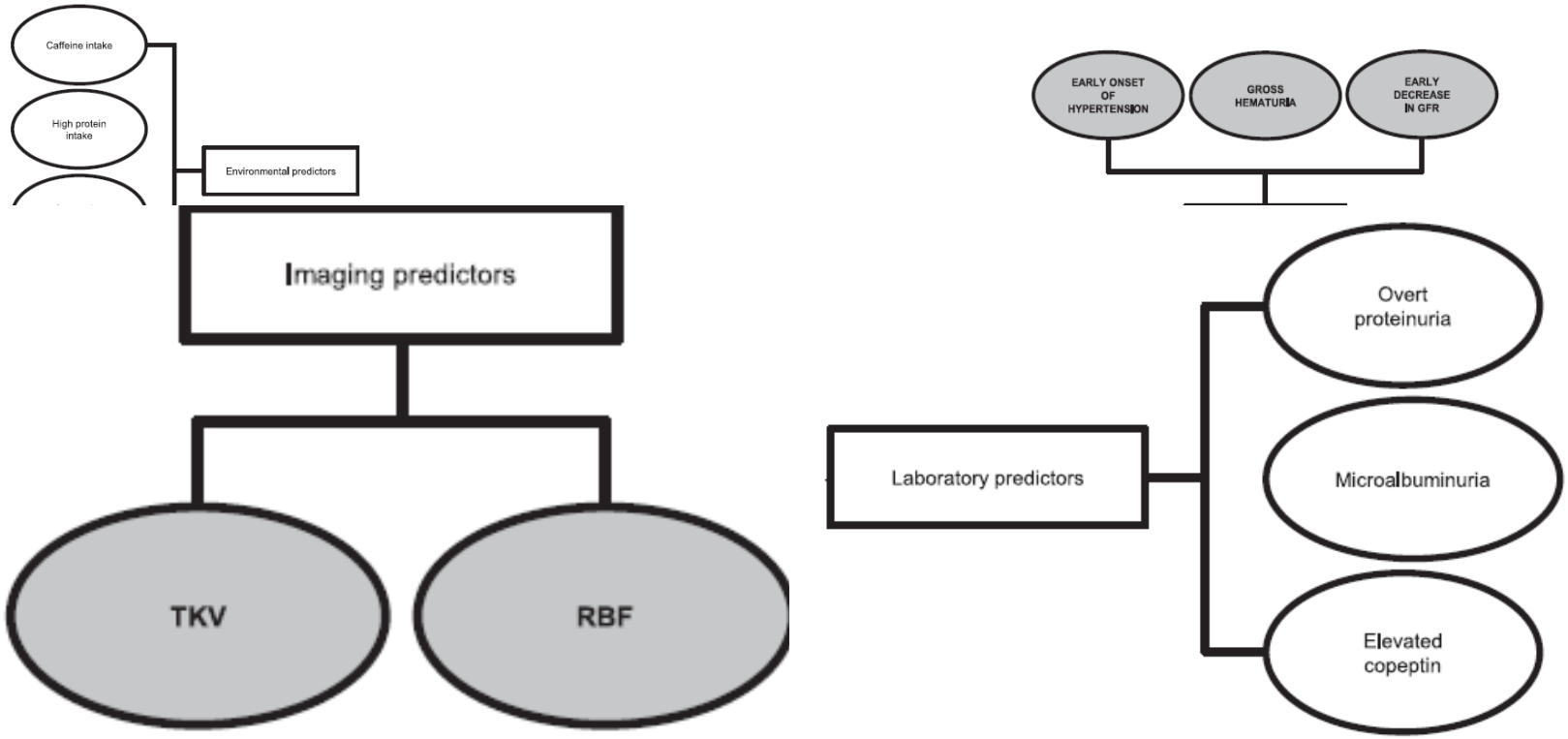
PKD Progression:
Systematic Review





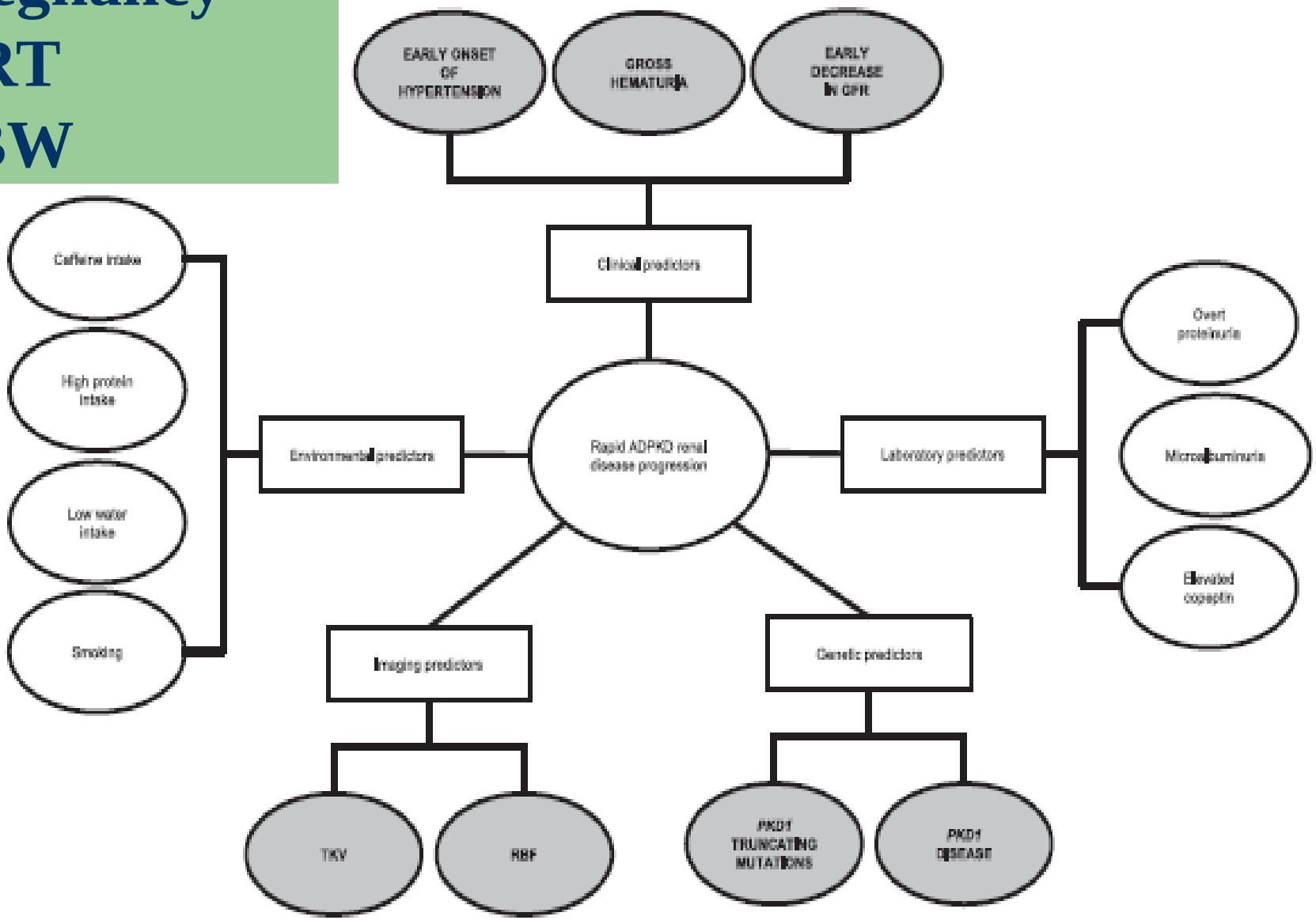
J Am Soc Nephrol 25: 2399–2418, November 2014.

PKD Progression:
Systematic Review



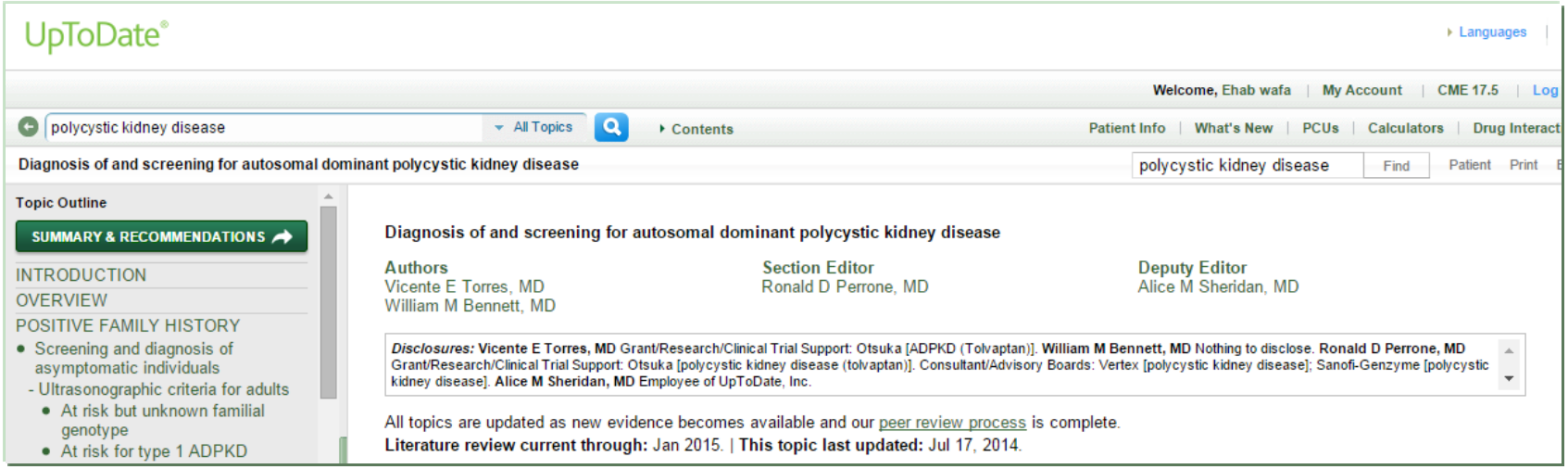
J Am Soc Nephrol 25: 2399–2418, November 2014.

Pregnancy
HRT
LBW



J Am Soc Nephrol 25: 2399–2418, November 2014.

Controversial Issues



Q1. Regarding Treating Hypertension in ADPCK: Which is Considered The Last Choice?

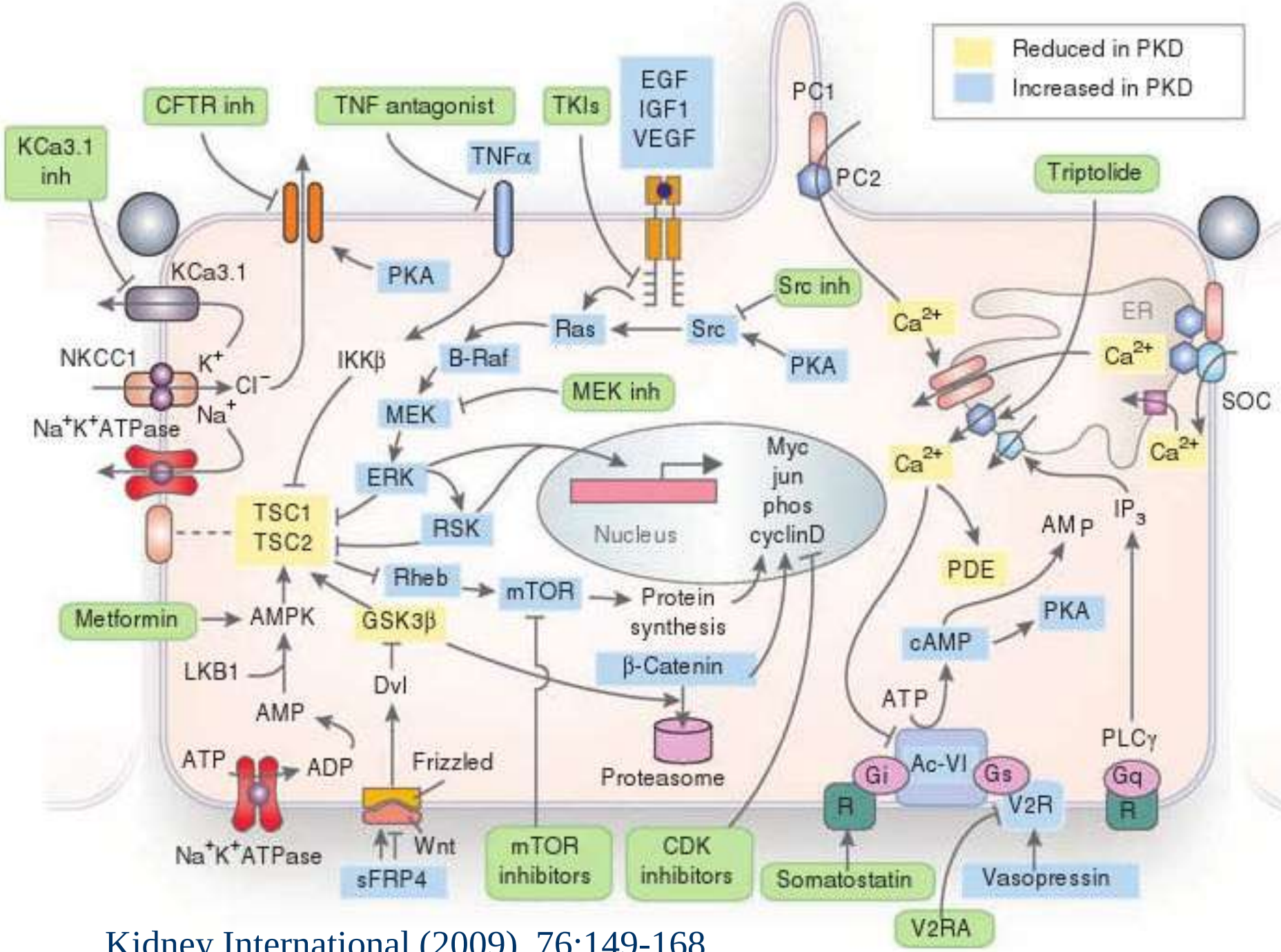
1. Angiotensin converting enzyme inhibitors
2. Angiotensin receptor blockers
3. Calcium channel blockers
4. Beta blockers
5. Diuretics

Q2. Regarding Treating ADPCKD: Which is the correct statement?

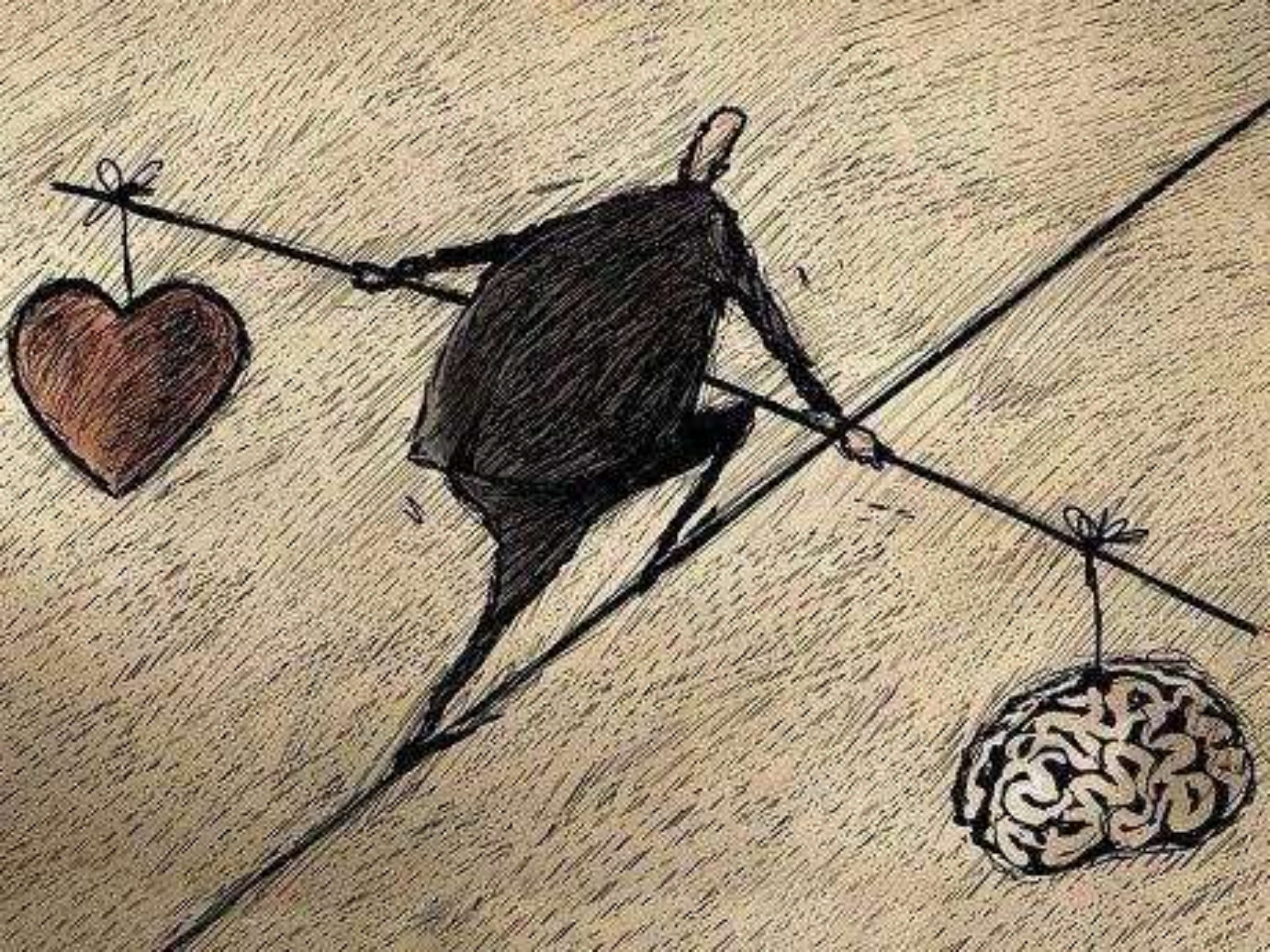
1. The beneficial effects of sirolimus appear after long-term use
2. Tolvaptan is recommended to reduce renal cysts
3. Even water drinking all through waking hours may reduce cyst growth
4. Long acting somatostatin is recommended
5. Tyrosine kinase inhibitors are safe and effective
6. Early screening improves the efficacy of sirolimus

Q3. For How Long Tolvaptan Therapy Is Safely Given?

1. 1 month
2. 3 month
3. 1 year
4. 3 years
5. 5 years



Kidney International (2009), 76:149-168.



Treatment of PCKD

A wise Physician said:

The best medicine for human is

Love & Care